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Weaning: Risk Factors for the Development of Overweight and Obesity in Childhood - A Systematic Review

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Abstract

Weaning practices including the age of the infant at time of weaning, nutritional composition of the weaning diet and rapid weight gain have been suggested to be risk factors for overweight and obesity in childhood. The purpose of this review was to investigate the relationship between weaning practices and overweight and obesity in childhood (from birth to 18yrs) and to identify the risk factors associated with weaning for overweight and obesity in childhood (birth to 18yrs). This was achieved through a systematic review of relevant literature, identified using a number of databases such as CINAHL, EMBASE, and MEDLINE and through searching individual journals. Inclusion criteria consisted of children's age 0-18yrs, details on stage of and weaning diet, studies published in English from 2000-2010 and human studies. The quality of the methodology of studies was assessed using the Downs & Black (1998) quality assessment tool. Thirteen studies out of an original 67 were included in the review. Study sizes varied from 90 to 10,553 subjects and quality assessment scores ranged from 14 to 23. All of the studies which considered the relationship between age at introduction of complementary foods and weight gain found those infants weaned before 16 weeks (wks) gained more weight than those weaned later; these findings were more significant in those infants who were not breastfed or breastfed for less than 4wks. One study (from 5) found a significant relationship between the age at introduction of complementary foods and overweight and obesity. Four studies (from 5) reported a significant relationship between nutritional composition of the weaning diet during the first year of life and overweight; the most significant effect being that of protein as a percentage of energy intake. The evidence for the impact of early weaning on adiposity levels, overweight and/ or obesity remains is inconsistent. Findings suggest that there is no relationship between adiposity and BMI in childhood with early weaning practices. However, the introduction of complementary foods before 16wks was shown to lead to greater weight gain in early childhood (independent of other confounding factors), especially in those infants who are fed formula food or is only breastfed for less than 4wks, which in turn could lead to overweight and obesity in later childhood. High protein intake (as percentage of energy) is strongly suggested to influence weight gain during infancy and BMI in early childhood.

Key Words: Complementary feeding, weight, weight gain, body mass index, nutrition, infant.

Declaration

This work is original and has not been previously submitted in support of a Degree, qualification or other course.

Signed:

Date:

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CHAPTER 1

INTRODUCTION

Obesity is not a new phenomenon and the extent to which it impacts on health and social factors are well known. However, the extent and rate of increase in both childhood and adult overweight and obesity is a cause for concern. Obesity is a complex, multifactorial condition influenced not only by physiological factors but also by attitudes, behaviours, economic and social drivers (Foresight, 2007); the potential determinants of overweight and obesity in children are illustrated in Figure 1 below. Genetic and metabolic factors, dietary and physical activity, breast and formula feeding, environmental factors and weaning will be discussed in more detail in later sections.

Figure 1: Potential Determinants of Overweight and Obesity in Children

Source: Monasta, Batty, Cattaneo, Lutje, Ronfani, van Lenthe & Brug, 2010.

A child is defined by the United Nations (1999) as '*every human being below the age of eighteen years unless under the law applicable to the child, majority is attained earlier'.* During this period a child undergoes rapid physical and emotional development, it is felt that during this period risks for the development of both overweight in childhood and adulthood exist.
The dramatic rise in childhood obesity has led to a number of studies looking at critical periods in the life course when the risk of developing obesity is increased (Owen, Martin, Whincup, Davey Smith & Cook, 2005; Owen, Martin, Whincupp, Davey-Smith, Gillman & Cook, 2005; Reilly, J.J., Armstrong, Dorosty, Emmett, Ness, Rogers, Steer & Sherriff, 2005). The relationship between breastfeeding and the prevention of overweight and obesity in children has been well documented (von Kries, Koletzko, Sauerwald, von Mutius, Barnet, & Grunet, 1999; Armstrong, 2002; Owen et al. 2005; Laurence, Grummer & Zuguo, 2004). However, few studies have focused on the weaning stage of the life course.

The aim of this systematic review is to investigate the relationship between the weaning stage of the life course and the risk of children (from birth to 18yrs) becoming overweight or obese.

CHAPTER 2

LITERATURE REVIEW

This section provides an overview of relevant literature relating to overweight and obesity in childhood. It includes information on definitions, prevalence and predicted trajectories and causes of overweight and obesity, which provided the evidence for the rationale of the study.

2.1 Definition of Overweight and Obesity

Overweight and obesity are defined as *'abnormal or excessive fat accumulation that may impair health'* (World Health Organisation (WHO), 2011).

Defining overweight and obesity in children is complicated by the fact that weight varies with height as children grow. There are several different methodologies for defining childhood obesity such as the 1990 UK Growth Body Mass Index (BMI) Charts using the 85th and 95th percentiles, which are used mainly in clinical settings and to define overweight and obesity at a population level (Cole, Freeman & Preece, 1995). The International Obesity Task Force (IOFT) definitions based on BMI, the tool identifies the childhood percentile and corresponds to a BMI of 25 or 30kg/m^2 (overweight and obese respectively) at 18yrs. It allows for international comparison and enables smooth transition from childhood to adulthood in terms of classification. (Cole, Bellizzi, Flegal & Dietz, 2000), and is mainly used for epidemiological purposes.

BMI is considered to be an appropriate measure of overweight and obesity in adults, but it does have limitations when used as a measure of overweight and obesity for both adults and children. BMI is a surrogate measure of body fatness and is more of an indicator of excess weight than actual body fatness. BMI does not differentiate between excess fat, muscle mass or bone mass and therefore, does not provide an indication of the distribution of fat in individuals. It also does not take into account the changes in body shape during the maturation process in children or in the case of adults the difference in the body composition during ageing process (older people tend to have more body fat than younger people at the same BMI) as well as the differences between both genders and ethnicity (CDC, 2011). Dehghan, Akhtar-Danesh & Merchant, 2005 discuss the main problems using BMI in children and state the main problem as being that BMI does not take into account fat and fat-free mass and the impact this may have in exaggerating the levels of overweight and obesity in larger muscular children. More recent studies have used Dual X ray absorptiometry (DEXA) scan as body weight is only partly due to differences in body fatness. DEXA is a technique for directly measuring adiposity and identifies the amount of fat mass and fat free mass and the results can then be analysed taking into account ethnicity (for example, black children, at any BMI level, have significantly higher percentage of lean mass than white children), gender and maturation. DEXA is considered to be the most accurate measure of adiposity in children, however DEXA is costly and is not easily accessible (Burdette, Whitaker, Hall & Daniels, 2006; Robinson, Marriott, Crozier, Harvey, Gale, Inskip, Baird, Law, Godfrey, Cooper & Southampton Women's Survey Study Group, 2009).

Due to the ease of use, body weight and the use of standard screening tools (such as growth percentiles charts, BMI growth charts) are considered to be appropriate tools to use to identify overweight and obesity in children. Due to the relatively small number of studies completed on the areas under review this systematic review is not limiting studies to those using the same definition of obesity, definitions used are detailed and discussed in later sections.

2.2 Scale of the Problem

Globally in 2010, approximately 45 million children under the age of 5 years (yrs) were overweight (using IOFT classification), the increase in overweight and obesity is now being seen in low and middle income countries, particularly in the urban setting (WHO, 2010). WHO also estimated that 92 million were at risk of becoming overweight and identified that the worldwide prevalence of childhood overweight and obesity increased from 4.2% (95% CI: 3.2%, 5.2%) in 1990 to 6.7% (95% CI: 5.6%, 7.7%) in 2010. This trend is expected to reach 9.1% (95% CI: 7.3%, 10.9%), or 60 million, in 2020. The International Association for the Study of Obesity (IASO) (2011) reported varying rates and methods of defining overweight across Europe, as shown in Table 1 overleaf.

Table 1: Overweight Children in the European Union

Source: IASO (2011)

To estimate levels of childhood overweight and obesity in the UK, the Foresight Report (2007) applied the IOTF classification to the raw data from the 2004 Health Survey for England. They identified that 10% of 6-10yr old boys and girls, 5% of 11-15yr old boys and 11% of 11-15yrs old girls were obese, for the under 20s age group as a whole they identifies that 10% of females and 8% of males were obese and a further 25% of females and 20% of males were overweight.

Recent data from the National Childhood Measurement Programme (The Information Centre, 2009), using UK 1990 growth reference charts (Cole, Freeman & Preece, 1995), shows that 21.8% of girls and 24.3% of boys in reception (age 4-5yrs) and 31.6% of girls and 35% of boys in year 6 (age 10-

11yrs) are either overweight or obese. Comparison data for boys and girls in Reception (4-5yrs) and Year 6 (10-11yrs) for the 3 yrs of this programme (The Information Centre 2008; 2009 & 2010) can be seen in Figures 2 and 3.

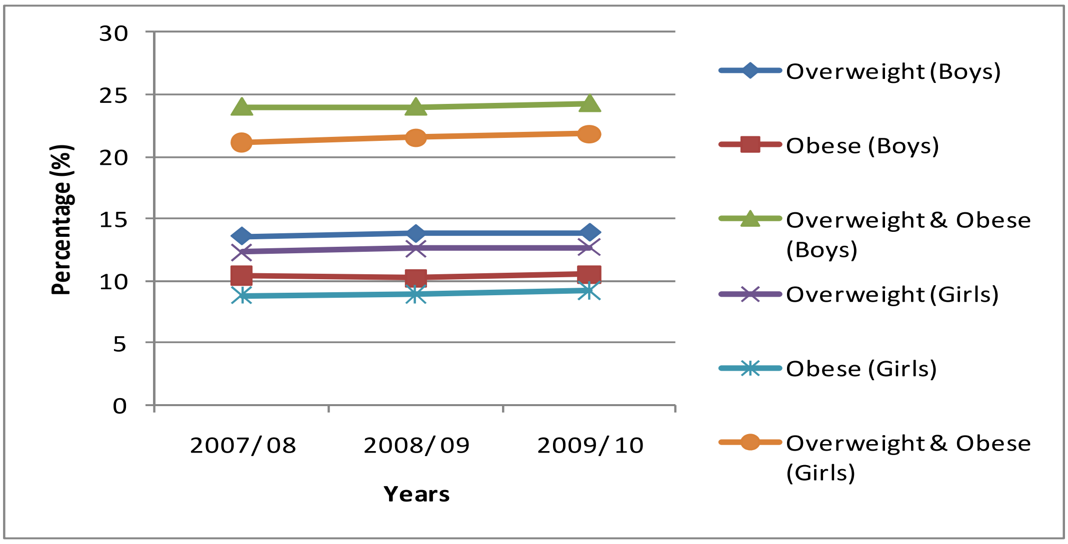

Figure 2: Comparison of Overweight and Obesity Rates for Boys and Girls in Reception for years 2007/08, 2008/09 and 2009/10

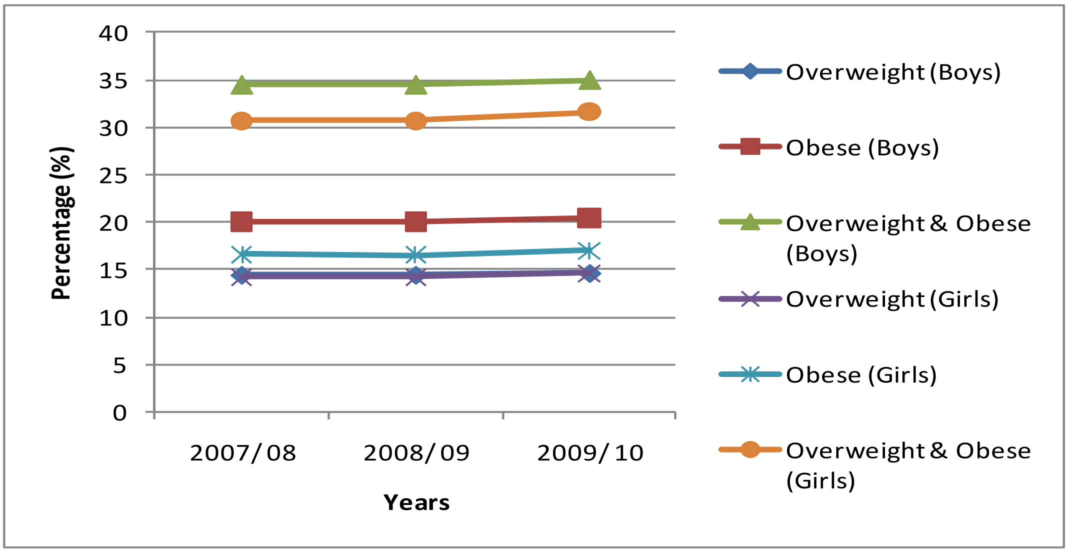

Figure 3: Comparison of Overweight and Obesity Rates for Boys and Girls in Year 6 for years 2007/08, 2008/09 and 2009/10

With this rise in childhood obesity there is an increase in many obesity related conditions once thought only to apply to adults. Conditions include high blood pressure, raised lipid profiles (dyslipidaemia), early symptoms of hardening of the arteries, fatty liver disease, polycystic ovary disease and Type 2 diabetes (Daniels, 2006; Freedman, Dietz, Srinvasan & Brenson, 1999; Srinivasan, Myers & Berenson, 2002). It is a well known hypothesis that children who are obese are more likely to become obese adults, and that obesity reduces life expectancy by an average of 9yrs (more when combined with smoking prevalence) (DH, 2006). If the rise in obesity continues as the Foresight project (2007) has predicted then 70% of girls and 55% of boys will be either overweight or obese by 2050. This increase will not just put extra burden on the health system but the economy as a whole. Foresight (2007) stated that in 2001, it was estimated that obesity cost the NHS £2billion/yr and the total impact on employment was as much as £10billion/yr (includes sick days etc). By 2050 the NHS costs of overweight and obesity could rise to £9.7billion/yr, with the wider societal costs being £49.9billion/yr. Table 2 shows a breakdown of where the increase could be seen (Foresight Project, 2007).

Table 2: Future Costs of Elevated BMI (adapted from the Foresight Report, 2007)

	2007 (£bill)	**2015 (£bill)**	**2025 (£bill)**	**2050 (£bill)**
Total NHS cost of diabetes	2	2.2	2.6	3.5
Total NHS cost of Coronary Heart Disease	3.9	4.7	5.5	6.1
Total NHS cost of Stroke	4.7	5.2	5.6	5.5
Total NHS cost of other related	6.8	7.4	7.8	7.8
Total costs (all related)	17.4	19.5	21.5	22.9
NHS cost attributable to elevated BMI	***4.2***	***6.3***	***8.3***	***9.7***
Wider costs of overweight and obesity	***15.8***	***27***	***37.2***	***49.9***

2.3 Causes of Overweight and Obesity

The cause of obesity is multifactorial; genetic and metabolic, diet and lifestyle factors, including infant feeding practices (breastfeeding/ formula feeding) and other environmental factors all have a role to play which has already been highlight by Figure 1 in Chapter 1, the next section considers some of the evidence surrounding these factors.

2.3.1 Genetic and Metabolic

Over the last decade there has been increasing research into the role of the brain centre and reward centres that regulate energy homeostasis, as well as, increasing interest into the role of gut hormones which have the ability to adapt pathways and result in satiety or stimulate appetite (Wynne, Stanley, McGowan & Bloom, 2005). Hansen, Dendale, Berger, van Loon & Meeusen, (2007) developed the 'thrifty gene' theory and have suggested that during the Palaeolithic period when food was scarce and individuals had high physical demands placed on them, calories were stored effectively so food stores could be metabolised when food was scare. It is thought that this hypothesis may explain the phenomenon of 'catch up growth' which occurs early in life after fetal, neonatal or infantile growth retardation and is now deemed a major risk factor for the later development of obesity (Dulloo, 2008). Wardle (2008) (as cited by Sheppard, 2009) proposes that BMI in children is highly inheritable.

A systematic review of systematic reviews by Monasta et al. (2010) supports this and reported that the review confirmed a significant heritability component of several anthropometric indexes including parental height, weight, BMI and percentage body fat. They also cite two studies which suggest that genetic factors account for 20-90% (Maes, Neale & Evans, 1997) and 40-70% (Farooqi & O'Rahilly, 2005). However, Rolls (2007) states that genetic factors cannot be blamed for the epidemic of obesity due to the timescale being too short, as the biggest increase in overweight and obesity having been seen since 1990.

2.3.2 Diet and Physical Activity

This section discusses the dietary and physical activity factors associated with older infants and children, with the aim of providing information on all factors considered to be determinants for childhood overweight and obesity. Information specifically related to weaning is discussed in section 2.4.

Dietary Factors

Changes in energy intake for both adults and children have been observed by Caballero (2007) in the United States (US). Popkin, Neilsen, & Siega-Riz (2002), Rajeshwari, Yang & Nicklas (2005), Striegel-Moore, Thompson & Afffenito (2006) (as cited by Caballero, 2007) found that energy intake in the US population (adults and children) has increased by approximately 200kcal/day over the past 20 years, this increase is from mainly 'empty calories' (foods that provide mainly energy and no other nutritional value e.g. sugar), which now accounts for 25% of the daily calories in young adults.

With respect to dietary factors, the National Diet and Nutrition Survey (NDNS) (2010) (a rolling programme looking at the consumption of food and nutritional intakes in the UK population (1.5yrs and over) via 4 day self reported dietary intake) found that for children (1.5yrs to 18yrs) there has been no change in total energy intake and cereal intake and a slight increase in the consumption of meat, meat products and meals (with the exception of toddlers) when compared to previous surveys. NDNS (2010) reported mean energy intakes for toddlers (1.5yrs to 3yrs) 1136Kcal (4.79Mj) with total fat contributing 40% and protein 14.5%-15.4% of energy for toddlers. The mean energy intake for boys and girls aged 4yrs -10yrs were 1591Kcal (6.71Mj) and 1523Kcal (6.41Mj) respectively, and for older children aged 11-18yrs are 2154Kcal (9.07Mj) for boys and 1668Kcal (7.02Mj) for girls. Fat intake as a percentage of energy for 4yr-10yr olds was 34% for boys and 35% for girls and for 11yrs-18yrs was 34% and 35.4% respectively for boys and girls. The percentage of energy from carbohydrates was 51.5% and 50.6% for boys and girls respectively and for 11yr-18yr olds was 50% and 49.4% for boys and girls respectively. Finally, the percentage of energy from protein for 4yr-10yrs old boys was 14.5% and 14.4% for girls and for boys and girls ages 11yr-18yrs was 14.6% and 14.4% respectively (NDNS, 2010).

Physical Activity

A longitudinal study of girls aged 9-18yrs in the US by Kimm, Glynn & Kriska (2002) (as cited by Caballero, 2007) found that physical activity levels have decreased across all age groups but in particular in girls aged 9yrs-18yrs of black origin. These findings in terms of the reduction in physical activity levels in the United Kingdom are supported by those of the Foresight Project Report (2007) and Canoy & Buchan (2007). Foresight (2007) do highlight that in terms of changes in physical activity levels for children this is less clear (despite a reduction in walking to school and cycling) as more often physical activity levels are estimated through work related activities. However, Canoy & Buchan (2007) cite Gortmaker, Must, Sobol, Peterson, Colditz & Dietz (1996) reported that in children a dose response relationship was seen between the numbers of hours watching television and the prevalence of obesity. UK Social Trends (2005) (as cited by Canoy & Buchan, 2007) support these findings and describe a reduction in the number of children walking to and from school (61% in 1992-94 to 53% in 2003) and an increase in car usage (from 30% to 39 % 1992-94 to 2003 respectively), questioning a relationship between these two factors and the increase in distance from home to school rising from 1.9km to 2.3km, and recommending further analysis to identify if such a relationship exists.

This demonstrates that there continues to be conflicting evidence regarding changes in dietary habits of children; this could be due to the problems of measuring dietary intakes outside of a laboratory setting (Foresight, 2007). The reduction in energy expenditure suggests that this could be the main contributory risk factor to the development of obesity if the simple explanation of energy balance is to be assumed (stable energy intake + reduction in energy expenditure = weight gain).

2.3.3 Breastfeeding and Formula Feeding

Many studies have looked at the relationship between breastfeeding and childhood obesity, evidence suggesting that there is a positive relationship between exclusive breastfeeding and children of normal weight (Kifsantas, & Gaffney, 2010; Rzehak, Sausenthalerm, Bauer, Schaaf, von Berg, Berdel, Borte, Herbarth, Kramer, Fenske, Winchmann, & Heinrich, 2009). This is felt to be due to the natural limits of energy supply in breast milk. The duration of exclusive breastfeeding has been found to have a positive inverse relationship with overweight and obesity. Robinson, Marriott, Crozier, Harvey, Gale, Inskip, Baird, Law, Godfrey, Cooper & Southampton Women Survey Study Group (2009) found that longer duration of breastfeeding (more than 12 months) was associated with lower fat mass at age 4yrs (measured via DEXA scan) when compared to those children who were never breastfed. These associations were independent and little changed following adjustment for confounding factors (sex, maternal age, BMI, height, education, social class, smoking in late pregnancy, infant birth weight and age at introduction of solids). However, this relationship is challenged by a number of studies, in particular when considering the relationship between obesity in late childhood and adolescence (Shields, Mamun, O'Callaghan, William & Najman, 2010; Neutzling, Hallal, Araujo, Horta, Vieira Mde, Menezers & Victoria, 2009; Kramer, Matush & Vanilovich, 2007). A meta analysis undertaken by Owen, Marton, Whincupp, Davey-Smith, Gillman, & Cook (2005) supported the evidence that a small protective effect of breastfeeding was seen but noted there was significant evidence of publication bias which possibly supports those findings of Shields et al. (2010), Neutzling et al. (2009) and Kramer et al. (2007).

2.3.4 Other Environmental Factors

Factors which effect individual’s choice and lifestyle such as parental work and leisure time, transport and town planning, food production and marketing, targeting of high fatty sugary cereals and treats during children’s television viewing hours have been linked to the rise in childhood overweight and obesity (Foresight, 2007).

2.4 What is Weaning?

Weaning can be defined as *‘the transition from an exclusively milk diet to a diet based on solid foods’* (National Institute of Clinical Excellence (NICE), 2008).

The European Society for Paediatric Gastroenterology, Hepatology and Nutrition Recommendations, 2008 (Agostoni, Decsi, Fewtrell, Goulet, Kolacek, Koletzko, Fleischer Michaelsen, Moreno, Puntis, Rigo, Shamir, Szajewska, Turck, & van Goudoever & North American Society for Pediatric Gastroenterology, Hepatology and Nutrition, 2008) reviewed the literature on complementary feeding for healthy term infants in 2008 and recommend that:

- Exclusive breastfeeding for 6 months is desirable;
- Weaning onto solid foods should begin by 6 months (mths) but not before 4 months;

- Breastfeeding should continue throughout weaning, particularly the early stages;
- Introducing gluten (wheat, rye, barley and oats, present in bread, wheat flour, some breakfast cereal and rusks), between 4mths and 7mths while breastfeeding may reduce the risk of coeliac disease, type 1 diabetes and wheat allergy;
- High allergen foods such as egg and fish do not need to be delayed until after 6mths as there is no evidence that this will reduce the likelihood of allergies.

UK policy currently promotes exclusive breastfeeding for the first 6mths of life, thereafter commencing onto a variety of foods of differing textures and flavours; weaning before six months is not recommended due to the digestive system not being fully developed as this can increases the risk of colic, constipation, infections and allergies (NICE, 2008). These guidelines are based on the consideration of the optimal duration of breastfeeding and the ability of breast milk to meet requirements for macro and micronutrients becoming limited as the child gets older. Guidance recommends the inclusion of foods from all of the five food groups and avoidance of high sugary foods/ salty foods, honey and whole nuts until the age of 5yrs (Shepherd, 2008).

2.5 Relationship between Weaning and Overweight and Obesity

2.5.1 Nutritional Composition of the Weaning Diet

McMaster (2006) found that introducing a child to a variety of foods, tastes and textures during weaning and early childhood can help a child to develop a more varied and balanced diet (as cited by Shepherd, 2009).

As with the dietary patterns of older children (1.5yrs to 18yrs, as described in section 2.3.2), the nutritional composition of the weaning diet has changed over time, with the introduction of expanding ranges of manufactured weaning products. Shepherd (2008) reviewed the evidence for optimal nutritional advice from pregnancy through infant feeding (breast, formula, breast + formula feeding), weaning and onto childhood and found that little is actually known about what constitutes an optimal diet in infancy and that there appear to be relatively few studies on weaning practices in the UK, therefore it is not possible to see what changes in energy and macronutrient intake have occurred over the years.

A prospective cohort study of 1740 infants which compared the growth of infants whose feeding patterns closely followed current guidelines with the growth of infants with other feeding patterns, found that infants whose dietary pattern was most similar to current feeding guidelines (with high consumption of fresh fruit and vegetables, home-prepared foods and breast milk), gained weight and skinfold thickness more rapidly from 6mth to 12mths than other infants, independent of milk feeding, age at introduction of solids and maternal factors. Compared with infants in the lowest quarter, infants in the highest 'infant guidelines' score quarter gained 0.24kg (95% CI 0.06, 0.43) in weight and 0.26 (95% CI 0.07, 0.45) in skinfold thickness (Baird, Poole, Robinson, Marriott, Godfrey, Cooper, Inskip, Law & Southampton's Women's Survey Study Group, 2008).

A body of evidence exists relating to the nutritional composition of the diet and metabolic factors associated to risk of overweight and obesity and early adiposity rebound.

Koletzo, Broekaert, Demmelmair, Franke, Hannibal, Oberle, Schiess, Baumann & Verwied-Jurky (2005), report that higher protein intakes in excess of metabolic requirements may enhance the secretion of insulin and insulin like growth factor 1 (IGF1). High insulin and IGF1 values can enhance both growth during the first two years of life and adipogenic activity and adipocyte differentiation. Hypothesising that *'a high protein intake with infant formula, in excess of metabolic requirements may predispose to an increase risk of obesity in later life'.*

The relationship between nutritional intake and early adiposity rebound has been identified by Rolland- Cachera, Deheegar, Maillot & Bellisle (2006) following a review of evidence. They reported that adiposity rebound normally occurs at approximately age six years and is related to overweight. A high protein, low energy diet in a time when an infant required higher energy intake was associated with this adiposity rebound.

This is contradicted by early findings of Dorosty, Emmett, Cowin, Reilly and the ALSPAC study team (1999) who undertook a longitudinal cohort study of 885 children from birth to five years in the UK. Dorosty et al. (1999) concluded that early adiposity was not related to high protein intakes or any other dietary variable.

2.5.2 Maternal and Family Characteristics Influencing Good Weaning Practices

Robinson, Marriott, Poole, Crozier, Borland, Lawrence, Law, Godfrey, Cooper, Inskip, and the Southampton Women's Survey Study Group (2007) have detailed the maternal and family characteristics and habits that influence weaning as being maternal food choices, maternal educational attainment and birth order (first born more likely to have diet inline with infant feeding guidelines defined by a high frequency of consumption of fruit, vegetables, meat, fish, other home prepared foods and greater consumption of breast milk, but low frequency of consumption of commercial baby foods in jars and lower consumption of formula milk).

2.5.3 Age and Rate of Weight Gain during Weaning

The UK 2005 Infant Feeding Survey (Bolling, Grant, Hamlyn, & Thornton, 2007) found that 51% of infants were reported to have received complementary foods before 4mths, and thus earlier than the previous UK recommendation for 4mths to 6mths (the other 49% are given solids between 4mths to 6mths). Parents perceive that their baby is ready to begin weaning earlier than 6 months (Fewtrell, Lucas & Morgan, 2003; Foote & Marriott, 2003; Bolling et al. (2007)).

Morgan, Lucas & Fewtrell (2004) examined the relationship between the age of introduction of solids and short and medium term health consequences in 1600 infants from 1993 to 1997. They found that those children weaned before the age of 12wks were heavier (5.68kg and 5.45kg, respectively, p=<0.001) and longer (59.04cm and 58.58cm respectively, p=0.01) at age of 12 wks than those weaned later than 12 wks, but weight and length at 12mths to 18mths were the same and conclude that there is little evidence to suggest that weaning before 12wks influences health outcomes up to 18mths.

These findings are supported by the findings of Ong, Emmett, Noble, Ness, Dunger, & ALSPAC Study Team (2006) who found that children being fed either breast or formula feed or a mixture of formula and breast milk and weaned before 4mths consumed significantly more energy. Energy intake at 4mths was also higher in infants who were given solid foods earlier (1–2 mths: 2805.6 +/- 50.4 kJ/day, n= 89; 2–3 mths: 2658.6 +/- 25.2 kJ/day, n = 339; 4= mths: 2587.2 +/- 46.2 kJ/day, n= 111). Higher total dietary energy intake at age 4mths was associated with greater gains in weight SDS between birth and ages 1yr, 2yrs, and 3yrs (P=0 .007 to P=0.0004) and with higher rates of rapid weight gain between 0 and 2 yrs (P=<0 .0001). These associations were found to be independent of current body weight and were seen amongst formula- or mixed-fed infants but not breastfed infants. Ong et al. (2006) concluded that dietary energy intake during infancy determines infant weight gain and may influence obesity risk during childhood, at least among formula- and mixed-fed infants

These findings are disputed by those of Carruth, Skinner, Hook & Moran (2000) who observed no significant association between introduction of complementary foods and weight and length at age 2mth to 8mth or 12mth to 24mth, in a cohort of 94 white mother infant pairs. As well as those of Mehta, Specker, Bartholmey, Giddens, and Ho (1998) who found no variation in growth of body composition between infants weaned early and those weaned late or the type of food consumed (infants in the commercial group consumed less protein calories at 9mths (80 ± 3 kcal/d vs 88 ± 3 kcal/d) and 12mths (101 ± 5 kcal/d vs 148 ± 5 kcal/d), less fat calories at 12mths (263 ± 10 kcal/d vs 343 ± 10 kcal/d), and less total calories at 12mths (884 ± 24 kcal/d vs 1022 ± 25 kcal/d) compared with the choice group). The early introduction of solid foods to an infant's diet does not alter growth or body composition during the first year of life and results in a displacement of energy intake from formula.

This literature review highlights the complexity in identifying the causes of overweight and obesity in childhood. It also identifies that there is a plethora of evidence focusing on breastfeeding versus formula feeding and the modifiable factors in later stages of childhood (nutritional intake, physical activity etc), the relationship between early nutritional intake and adiposity rebound, and that there is a gap in the understanding of the factors during the introduction of solids (weaning) and the impact this may have on risk of a child becoming overweight or obese.

CHAPTER 3

RATIONALE AND AIM OF REVIEW

Weaning practices including the age of the infant at time of weaning, nutritional composition of the weaning diet and rapid weight gain have been suggested to be risk factors for overweight and obesity in childhood. The purpose of this review is to investigate the relationship between weaning practices and overweight and obesity in childhood (from birth to 18yrs) and to identify the risk factors associated with weaning for overweight and obesity in childhood (birth to 18yrs). Achieved through a systematic review of relevant published studies which complied with the selection and exclusion criteria (described in Chapter 4), and through using an adapted version of the Downs & Black (1998) assessment tool to assess the quality of the methodology of the studies.

The findings of existing studies on the relationship between weaning and childhood overweight and obesity were analysed to determine if any provide information regarding the research question posed below:

- Does the age of weaning increase risk of childhood overweight and obesity?
- Are there differences in the nutritional composition of the weaning diet which increase the risk of childhood overweight and obesity?
- Does the rate of weight gain during weaning impact on childhood overweight and obesity?

CHAPTER 4

METHODOLOGY

This section describes the search strategy used by explaining the methods by which the research papers/ articles were searched, selected and evaluated; ensuring relevant articles are located and assessed for quality. The quality of the papers was assessed using the Downs and Black checklist for assessing quality (Downs & Black, 1998) (see Appendix A). This checklist was chosen as it assesses both randomised and non-randomised studies for quality of reporting, internal validity, external validity and power.

4.1 Search Strategy - Keywords and Terms

Keywords and search terms used to identify relevant articles can be seen in Table 3.

Table 3: Keywords and Related Search Terms Used to Identify Relevant Articles

Weaning	Weight	Age
Diet	Obesity	Infants
Nutritional Composition	Overweight	Children
Food	Weight	Adolescents
Meal Frequency	Body Mass Index (BMI)	School Children
Macronutrients	Body Fat	

These search words were combined using Boolean search operators of ‘AND’, ‘OR’ and ‘NOT’. For example:

Childhood obesity ‘AND’ weaning;

Nutritional Composition ‘AND’ weaning ‘AND’ obesity;

‘NOT’ animal studies.

4.2 Study Designs Searched

Observational studies were searched; these studies observe the interventions, exposures and outcomes within a population (with or without randomisation) rather than the interventions being prescribed by the researcher.

4.3 Database and Journal Searches

The keywords and search terms were used to search general and specific databases, general search engines and specific journals. Initially, the search focused on general and specific databases, then general search engines followed by specific journals, to ensure that all possible studies were retrieved.

Databases used were:

- BRITISH NURSING INDEX (BNI) – UK nursing and midwifery database, covering over 240 UK journals and other English language titles, including international nursing and midwifery journals, as well as selective content from medical, allied health and management titles, from 1985 to present day;
- CINAHL - covers all aspects of nursing and allied health disciplines from 1981 to present day;

- EMBASE – comprises of over 3500 international journals providing current and comprehensive information on drugs and pharmacology, and all other aspects of human medicine and related disciplines, from 1980 to present day;
- MEDLINE from PubMed - is a service of the U.S. National Library of Medicine that includes over 17 million citations from MEDLINE and other life science journals for biomedical articles, from 1950 to present day.

General search engines used:

- GOOGLE SCHOLAR – enables searches across many disciplines and sources (articles, theses, books, abstracts and court opinions, from academic publishers, professional societies, online repositories, universities and other web sites).

Specific journals searched:

- American Journal of Clinical Nutrition;
- British Journal of Nutrition and Dietetics;
- British Medical Journal;
- International Journal of Obesity;
- Journal of Nutrition;
- Journal of Clinical Endocrinology and Metabolism;
- Lancet;
- Obesity Reviews;
- Public Health Nutrition.

Finally, the reference lists of those published articles identified were used to ensure a comprehensive search of all available literature was conducted.

An independent search was undertaken using the search terms by the researcher and the librarian at Dorset County Hospital Foundation Trust to ensure appropriateness of search terms, consistency within the search and that relevant article's were not missed. This search using Medline highlighted slight variations in the citations found between the searches despite using the same search terms and this was related to the use of the Boolean search operators.

4.4 Article Retrieval

Following identification of relevant articles, full text articles were retrieved. It was anticipated that the majority of articles would be available through subscription free journals through one of the databases used. However, if the journal was not a subscription free journal then a search of the University of Chester electronic resources catalogue and Dorset County Hospitals Library took take place to see if it could be retrieved through either the University or Hospital Library. Inter library loan requests for the relevant journals took place through the inter library loan service provided by Dorset County Hospital Foundation Trust library service as well as purchasing individual articles direct from the relevant journal.

4.5 Selection and Exclusion Criteria

To enable studies to be included within the review they had to satisfy the following criteria:

- Studies will include detail of weight or BMI within the following age range 0-18yrs;
- Studies will provide stage of and details of the weaning diet, including age of weaning, nutritional composition and meal frequency;
- Studies will be published in English between 2000 to 2011 (to ensure that only the most recently studies are identified); and
- Human studies only (not animal).

It should be noted that one study may not provide all of the above information and it was necessary to review relevant studies together, for example, some studies may look at meal frequency and its relationship with childhood overweight and obesity and others nutritional composition of the weaning diet and the relationship with childhood overweight and obesity. Studies that did not meet the above criteria were excluded from the review.

4.6 Assessment of Quality

There are many checklists/ quality assessment tools available to assess the quality of the methodology used for published articles. However, these checklists have, in the main, been developed to assess randomised control trails (RCTs); for example, Jadad Assessment (Jadad, Moore & Carroll, 1996), which are a series of statements which can be scored to assess bias within a randomised control trial.

Downs and Black (1998) developed a checklist that it is able to assess the quality of both randomised and non-randomised control studies for quality of reporting, internal validity, external validity and power through a series of 27 questions. The checklist was developed based on epidemiologic principles, reviews and existing checklists for randomised control trials. It was initially assessed by experienced reviewers using 10 randomised and 10 non-randomised trials. Following this it was revised and retested using different raters to assess internal consistency and inter-rater reliability, criterion validity and respondent burden.

The revised Quality Index had high internal consistency (KR-20:0.89), therefore showing the tool had good precision with the exception of external validity (KR-20:0.54) (showing ability of the study to be generalised to the population). There were three main reasons for this, i) small number of questions compared to the other subscales (3 compared to 6-10), ii) possible lack of clarity of the question, and finally iii) poor interpretation by the reviewers; which was felt to be the most likely reason for the outcome (Downs & Black, 1998). Downs and Black (1998) also found that the test – retest and inter rater reliability was good (r-0.88 and r-0.75 respectively), therefore showing that there is consistency between the reviewers using the checklist.

The checklist enabled each article to score a maximum of 32 points through most questions scoring either 1= yes or 0=no, the exceptions are for question 5 (confounding factors) where it was possible that some details on confounding factors would be available but not all and there a partial score was added (yes=2, partial=1 and no=0); and question 27 which relates to power and could score 0-5points. Due to the power calculation methodology being unavailable the question was adapted so that 1 point was given if the article under review mentioned the power calculation and 0 if it did not. A worked example of the Downs and Black assessment tool can be seen in Table 4; this table also shows the comparison of assessment by the researcher and colleague.

Table 4: Quality Assessment Using Downs & Black Assessment Tool

Author	Date	Reporting (max 11)	Eternal Validity (max 3)	Bias (max 7)	Confounding (max 6)	Power (max 1)
Robinson et al (1*)	2009	10	2	4	4	0
Robinson et al (2*)	2009	9	2	4	4	0
Sloan et al (1*)	2007	9	2	3	4	0
Sloan et al (2*)	2007	9	2	3	4	0

* Key: 1- reviewer 1; 2- reviewer 2.

The two papers selected for the purpose of demonstrating the quality assessment process of the Downs and Black assessment tool (1998) are firstly a study by Robinson, Marriott, Crozier, Harvey, Gale, Inskip, Baird, Law, Godfrey, Cooper and Southampton's Women's Survey Study Group (2009) who looked at how variations in milk feeding and the weaning diet related to body composition at age 4yrs. Secondly, a study by Sloan, Gildea, Stewart, Sneddon and Iwaniec who looked at the effect on weight and weight gain in two groups of infants, those weaned before 4 months and those weaned after 4 months. Both these studies will be reviewed in detail in Chapter 5.

The quality assessment process highlighted no differences in the assessment of quality of Robinson et al. (2009) and Sloan et al. (2007), both studies clearly detailed the methodology used, confounding factors and detailed both standard deviation and probability values.

With respect to external validity neither study detailed differences in the confounding factors of the whole study sample compared to the source population.

As both studies were prospective cohort studies the three of the questions to assess bias were not applicable as two questions were related to randomised control trials and there was no intervention group in either study, therefore score 0 for each of the three questions.

Neither study detailed power and therefore scored 0.

To ensure user reliability both studies were assessed by the researcher and a colleague (senior information analyst). The only variation between reviewer 1 and 2 was the question relating to reporting of adverse events, this variation was due to misinterpretation of the question.

The test reviews did highlight that there could be misinterpretation of *question 4: 'are the interventions of interest described'* as most would consider only RCTs to have defined interventions where in this case an intervention was considered to be observational test groups (e.g. those weaned before 16wks) and the comparison group (e.g. those weaned after 16wks) as the intervention.

As the studies identified were cohort and case control trials the Downs & Black assessment tool (Downs & Black, 1998) was chosen to assess the quality of the methodologies of the studies, it was also had a clear framework and was simple to use.

4.7 Data Analysis

Due to the variety of studies included in this systematic review and the studies having different approaches, variations occur in terms of objectives, study designs, findings and presentation of findings, it is important to have a method for reviewing studies, data extraction and presentation. To ensure clear presentation of the results the following data was extracted from the studies reviewed and will be presented in the results sections:

1. Author and date;
2. Number and gender of subjects;
3. Classification of overweight/ obesity used;
4. Measurements taken;
5. Number of children weaned early (age at introduction of solids);
6. Nutritional composition of weaning diet;
7. Weight gain (kg);
8. Key findings;
9. Downs & Black score.

With respect to points, 3-9 the following paragraphs (1-7) provide clarity for their inclusion in the data collection.

1. (3) Classification of overweight/ obesity

   As highlighted in Chapter 2, section 2.1, overweight and obesity in children can be defined in a number of ways. The definition used within the studies was documented and if not stated due to the study not looking at overweight/ obesity per se (e.g. the study may consider weight gain) this was be documented as not applicable (n/a).

2. (4) Measurements taken

   This refers to the measurements taken to define overweight/ obesity, body composition (body fat, fat free mass etc) and growth as there are several different techniques used with different levels of reliability and accuracy as mentioned in Chapter 2 (e.g. dual xray absorptiometry (DEXA), skinfold thickness callipers).

3. (5) Age at introduction of solids

   As weaning recommendations/ guidelines vary across the world and with changes in national policy the number of children considered to be weaned early was recorded.

4. (6) Nutritional composition of the weaning diet

   This refers to the macronutrient content of the weaning diet and was broken down into sub sets of total energy (kJ), dietary protein (% of total energy and g/day), dietary fat (% of total energy and g/day) and dietary carbohydrate (% of total energy).

5. (7) Weight gain (kg)

   Refers to the amount of weight gained during weaning period this is considered in relation to either the age of the introduction of complementary foods or to the nutritional composition of the weaning diet.

6. (8) Key findings

   This refers to those results considered to be statistically significant, with significance set at 95% ($p < 0.05$).

7. (9) Downs and Black score

   To enable comparison of the studies in terms of quality the Downs and Black assessment score was also included. As previously mentioned (Chapter 4, section 4.6) this tool enables quality assessment (reporting, internal and external validity and power) of both randomised and non randomised studies.

To ensure the aims and objectives of this systematic review are achieved and the study questions are answered, the studies are divided in terms of their study objectives as follows:

1. Effect of the age of weaning on weight gain and/ or overweight/ obesity in children.
2. Effect of the nutritional composition of the weaning diet on weight gain/ and/ or overweight/ obesity in children.

CHAPTER 5

RESULTS

This section of the report presents the data from the original studies to enable the questions put forward in the rationale for this systematic review to be answered. Further information regarding the studies which have been included in the review can be seen in Appendix B; the below list indicates the information available:

1. Location and funding;
2. Objectives of the study;
3. Study design;
4. Number and description of the subjects;
5. Variables measured;
6. Age at measurement;
7. Definition of obesity;
8. Duration of the study;
9. Statistics analysed;
10. Results;
11. Conclusion.

5.1 General Characteristics

Following and initial literature search as outlined in Chapter 4, 67 original articles were indentified through the literature search as being relevant. Of these 29 (43.3%) did not meet the inclusion criteria as they considered general risk in terms of infant feeding or risks throughout childhood; eight (11.9%) focussed on breast versus formula feeding; six (8.9%) were either letters, editorials or systematic reviews and four (5.9%) were lecture notes from seminars. Of the remaining 20 (30%) original articles indentified, 13 (65%) were used within the review, the remaining seven (35%) were excluded, and the rationales for these exclusions are detailed below:

- Three were excluded due to the cost and time required for the local hospital library (Dorset County Hospital Foundation Trust) to obtain them from the National Library, London (Chivers, Hands, Parker, Bullsara, Beilin, Kendall, & Oddy, 2010; Harrington, Nguyen, Paulson, Garland, Pasquinelli, & Lewis, 2009; Kain, Corvalan, Lera, Galvan, & Uauy, 2010).

- Four were excluded as the full text article was not available and therefore only the abstract was available (Dubois & Girard, 2006; Gardiner, Hosking, Metcalf, Jeffery, Voss & Wilkin, 2009; Al-Qaoud, Prakash, 2009; Lamb, Dabelea, Yin, Ogden, Klingensmith, Rewers, Norris, 2010).

All studies reviewed were published in English during the period from 2000 to 2011. Six of the studies focussed on the age at the introduction of solid foods on weight gain and or overweight/ obesity in childhood, four focussed on the nutritional composition of the diet and weight gain and/ or overweight/ obesity in childhood and three studies covered both aspects.

The majority of studies were undertaken in Europe (nine), three in USA and one in South America, Figure 4 illustrates the countries where the studies were carried out. Twelve (92.3%) of the studies were cohort studies and one (7.7%) was a case control.

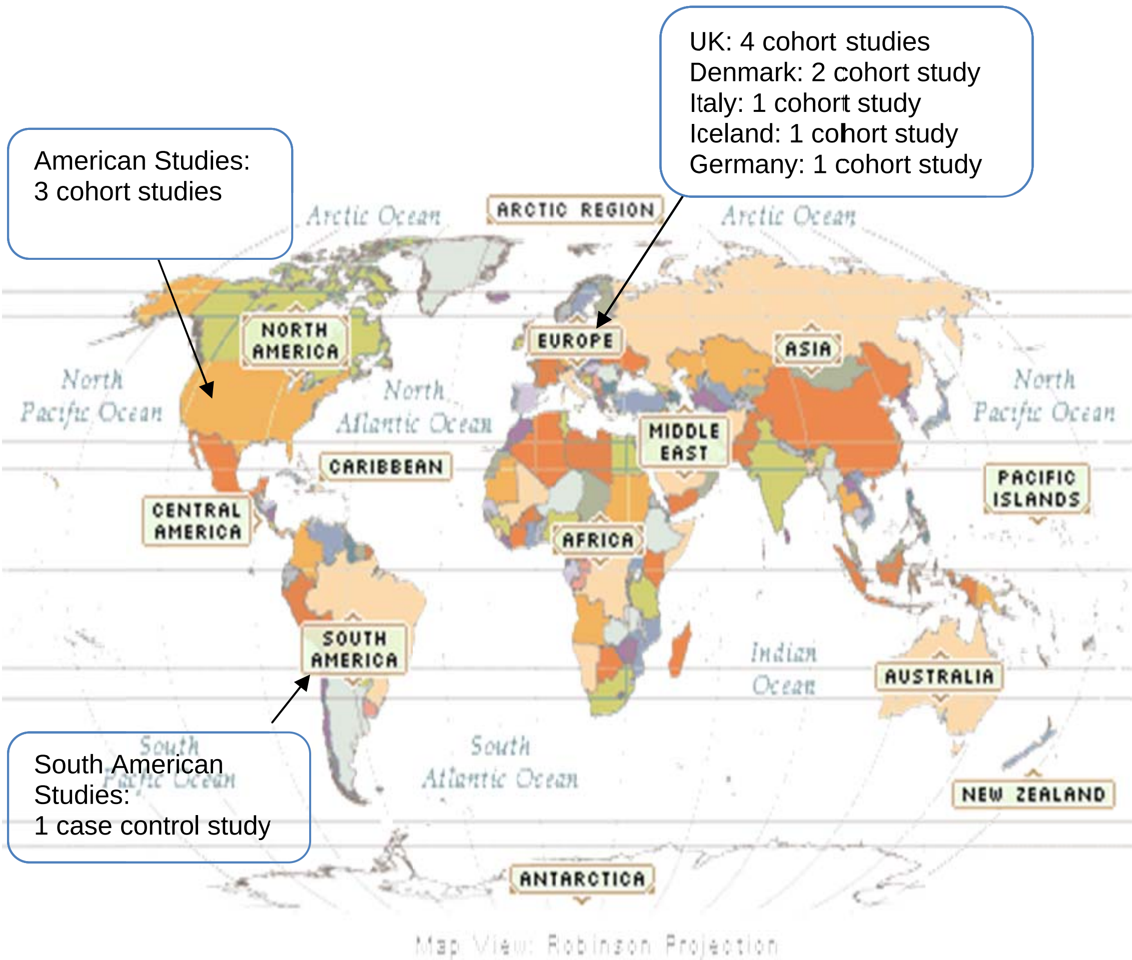

Figure 4: Location of studies in the review of impact of the weaning diet on the risk of childhood overweight and obesity (Source of map: http://www.infoplease.com/atlas)

As mentioned in section 4.6, the quality of the studies was assessed using Downs and Black assessment tool (Downs & Black, 1998) (Appendix A). The tool has 27 questions with a possible total score of 31. All the answers were scored 0 or 1 with the exception of questions 5 and 27 score either 1 point for yes or 0 for no. Question 5 which focuses on confounding factors scored as follows: yes=2 points, partially= 1 point and no= 0 points. Question 27 referring to ‘power’ (of the tool) was adapted so that the score for power was given as ‘1’ if the power of the study was considered and ‘0’ if not (rather than 0-5 as in the original tool); the total maximum score that could be awarded was 28. Scores given ranged from 14 to 23 (1=14, 1=17, 1=18, 3=19, 2=20, 3=21, 1=22, and 1=23), the score given to each study can be seen in Tables 5 and 6.

The study sizes varied from 90 to 10,553 participants; seven (53.8%) studies had less than 500 participants, two (15.4%) studies had between 500-1000 participants, two (15.4%) had between 1001 and 5000 participants and two (15.4%) had more than 5001 participants. All included both genders (male and female) and participants were 10yrs of age or younger.

The reviewed studies have been separated into two main categories in order to present the findings in clear and logical manner. The initial section (section 5.2) focuses on the age of weaning and the effect this has on weight gain and/ or overweight/ obesity in children and the subsequent section (section 5.3) focuses on the effect the nutrition composition of the weaning diet has on weight gain and/ or overweight and obesity in children. Three of the studies which investigated both the age of weaning and the nutritional composition of the weaning diet; these findings are reported in both corresponding sections.

5.2 Age of Weaning and the Effect this has on Weight Gain and/ or Overweight/ Obesity in Children

This section details the analysis of studies or aspects of studies which have investigated the age at which complementary foods (weaning diet) are introduced and the effect this has on weight gain and/ or overweight and obesity in children. The weight gain and weight parameters measured in the studies were weight, height or length, weight gain, skinfold thickness measurements and DEXA.

The results will be presented in chronological order based on date of the study.

Table 5, illustrates the study design, subjects, classification of overweight/ obesity used, measurements taken, number of children weaned early, the main outcomes and findings on the age of weaning and weight gain or overweight/ obesity in childhood.

Table 5: Age of Weaning- Effects on Weight Gain and/ or Overweight/ Obesity in Children

Author & Date	Location	Down's & Black Score	Study Design	Subjects (n)[a]	Overweight/ Obesity Classification [b]	Measurements [c]	Number of children weaned early and Age of Weaning (wks/mths)	Significance (or alternative)[d]	Findings [e]
Baker et al. 2004	Denmark	17	Prospective, observational cohort	3768 1902 males; 1866 females Age 1yr	N/A	Weight (g) Length (cm)	2072 16wks	Early weaning and infant weight gain at 1yr p=0.0021	Infants who were fed complementary foods before16wks compared with those who were fed after 16wks gained 224.2g more from birth to 1 yr.
Reilly et al. 2005	UK	19	Prospective birth cohort	8234- 3934 males, 3824 females from UK. Age 7yrs	1990 growth references- Obesity: >95th centile	Weight (kg); Height (m)	<1mth: 17; 1 or 2mth: 12; 2 or 3mth: 77; 3 or 4 mth: 320; 4-6mth: 134.	Introduction of solids: p=0.003 (adjusted p=296).	Following adjustment, the timing of the introduction of complementary food was not independently associated with the risk of obesity at age 7. Dietary patterns- no conclusive evidence of an association with dietary patterns at age 3 and risk of obesity at age 7. A junk food type diet was associated with risk of obesity at age 7 (although on to significance level of 10% p=0.83).
Burdette et al. 2006	USA	19	Cohort	313 preschool children- 166 males of which 24 black), 147 (of which 40 black) females. Age 5yrs	Overweight=>85th percentile; BMI measured kg/m^2. Centre for Disease Control (CDC) Classification 2000	Fat Mass- though Duel Energy X ray Absorptiometry; Height (m); Weight (kg); BMI- percentile and z score.	156 children < 16weeks	breastfeeding, formula feeding and use of complementary foods in first 4mths (16wks): never breastfed: p= 0.51; Partially breastfed: p= 0.39; Exclusively breastfed: p=0.45.	No significant relationship between adiposity (DEXA) at age 5yrs and either breastfeeding or the timing of the introduction of complementary foods (following adjustment for cofounders).
Sloan et al. 2007	Northern Ireland (UK)	18	Cohort	234 children 119 males, 115 females; Aged 0-18mths	N/A	Weight Weight Gain	92 children <16wks	birth z score: p=0.150; 8 week: p=0.555; 7mths: p=0.005 *(adjustment- p=0.046)* ; 14mth: p=0.004 *(adjustment= p=0.035)* ; 8wk-14mth wt gain: p=0.003 *(adjustment-p= 0.029)*	Infants weaned early had higher weight z scores at age 7months and 14months. Early weaning related in greater weight gain between 8weeks and 14months.

Table 5: Age of Weaning- Effects on Weight Gain and/ or Overweight/ Obesity in Children continued

Author & Date	Location	Down's & Black Score	Study Design	Subjects (n)[a]	Overweight/ Obesity Classification [b]	Measurements [c]	Number of children weaned early and Age of Weaning (wks/mths)	Significance (or alternative)[d]	Findings [e]
Robinson et al. 2009	UK	20	Prospective birth cohort	536 children 283 males, 253 females; Aged 4yrs	Overweight: BMI $>25kg/m^2$; Obese: BMI $>30kg/m^2$ (International Obesity Task Force)	Dual X ray absorptiometry; Weight (kg); Height (m); BMI (kg/m2)	536 <6mths Mean age of introduction 17.5 wks	Fat mass at age 4 and age of introduction of solids: p=0.034 (adjustment- not significant). Infant feeding guideline score and lean mass (kg): P=0.001 (adjustment p=0.003); Infant feeding guideline score and lean mass index (kg/m^2): P=0.011 (adjustment p=0.004).	No association between infant feeding guideline scores and BMI, fat mass, or fat mass index at age 4yrs. Lean mass and lean mass index positively associated with high infant feeding scores (diet based on fruit and vegetables, cooked meat and fish and other home prepared foods). Increased duration of breastfeeding (later weaning) associated with lower fat mass. No association between infant diet and mean BMI at age 4yrs.
Griffiths el al. 2009	UK	21	Prospective birth cohort	10,553 children- 5295 males, 5239 females; Aged 3yrs	1990 growth references	Weight (kg); Height (m)	4134 (39%)	Solids before 4 mths: p= <0.001 (adjusted p=0.003).	Conditional weight gain was associated with age at the introduction of solids (following additional adjustment for height association no longer existed).
Balaban et al. 2010	South America	20	Case Control	366 children 176 male; 190 female; Aged 2-6yrs	85th percentiles for weight (CDC, US growth reference charts,2000)	Height; Weight; BMI calculated	132 <16wks	Early weaning (<16wks) compared to >16wks) p=0.02 (unadjusted) (p=0.17 adjusted).	The association between early weaning (receiving exclusive or predominant breastfeeding for less than 16wks) and overweight did not reach statistical significance following multivariate analysis.

Table 5: Age of Weaning- Effects on Weight Gain and/ or Overweight/ Obesity in Children continued

Author & Date	Location	Down's & Black Score	Study Design	Subjects (n)[a]	Overweight/ Obesity Classification [b]	Measurements [c]	Number of children weaned early and Age of Weaning (wks/mths)	Significance (or alternative)[d]	Findings [e]
Huh et al. 2011	USA	19	Prospective birth cohort	847 children 421 males; 426 females Aged 3yrs.	Obesity: 95th percentile (CDC US growth charts, 2000)	Length; Height; Skinfold thickness	134 <16wks	Adjusted: Formula fed <16wks: OR: 6.3 (2.3-16.9) of obesity at 3yrs; BMI z score: 0.36 (0.10-0.61); Sum of triceps and subscapular skinfolds: 1.03 (-0.12-2.18). Breastfed <16wks: OR: 1.1 (0.3-4.4) of obesity at 3yrs; BMI z score: -0.19 (-0.49-0.11); Sum of triceps and subscapular skinfolds: -0.19 (-1.42-1.04).	For those infants never breastfed or stopped breastfeeding before 4mths of age introduction of solids was associated with a 6 fold increased odds of obesity at 3yrs of age. For those breastfed infants who were fed longer than 4mths timing of solids introduction was not associated with the odds of obesity.

a : Subject (males/ females and author classification if appropriate).
b : Classification of overweight/ obesity used in relevant studies.
c : Refers to the key measurements taken as part of the study, for example, weight, weight gain, DEXA scan.
d : States the key findings for the study which are significant (p= <0.05).
e: Describes the key findings of the study.

5.2.1 Age of Weaning and Weight Gain

The earliest study in this review was that of Baker, Michaelsen, Rasmussen & Sorensen (2004), who examined the relationship between infant feeding practices and weight gain. This was the first study to examine the effects of maternal prepregnant BMI, duration of breastfeeding and timing of complementary feeding simultaneously on infant growth, in a cohort of infants who were breastfed for long periods.

The study involved 3768 mother infant pairs from the Danish National Birth Cohort study (DNBC). Subjects were identified to take part in the study at their 12wk maternity visit and were required to speak Danish, those mother infant pairs who had never breastfed were excluded (these made up less than 1% of the population sample). Variables were assessed at 12wk and 26wk gestation and 6mth and 18mth postpartum via structured interviews over the telephone by trained professionals. Variables were categorised as maternal variables (social economic status (SES), educational attainment, age, occupation, parity, self reported height and weight) as well as maternal health conditions (alcohol consumption, smoking habits during pregnancy and gestational weight gain), infant variables (feeding practices and duration of breastfeeding, use of formula feeding (including duration) and introduction of complementary foods). Infant weight at birth was obtained retrospectively from the birth registry and weight and length at 1yr from the green book (infants own health record completed by GP) at 18mth interview and weight gain calculated from infants weight at doctors 1yr visit minus birth weight.

Baker et al. (2004) found that on average 55% of mothers had given complementary foods by 16wks and 99% by 24wks, at the time of the study the Danish Government's recommendations were that complementary foods should be introduced around 16wks to 26wks. Relationships were seen between the duration of breastfeeding and age at introduction of complementary foods; those mothers who breastfed their children longest, introduced complementary foods significantly later than those who 'ever fed' formula (had given formula feeds) and breastfed for the same duration On average those mothers who breastfed their children from 32wks to 40wks introduced solids 0.8wks earlier (p=<0.0001) compared to those who breast fed for more than 40wks and those mothers who fed formula foods (and breastfed) introduced solids 1.4wks earlier (p=<0.0001).

With respect to weight gain, Baker et al. (2004) found that those children who were fed complementary foods before 16wks gained 224.2g more from birth to 1yr than those who were fed complementary foods after 16wks (p=0.0001). An association between the duration of breastfeeding and weight gained from birth to 1yr; those breastfed before 40wks gained 317.4g more than those breastfed for after 40wks (p=0.0001). In an attempt to determine if the categories of 'any' breastfeeding (BF) duration and age at the introduction of complementary food (CF) explained the variance in weight gain at 1yr, these variables were introduced into the linear models. Significance was reduced but still remain significant effect was seen (CF before 16wks wt gain= 175.2g, p=0.0011; BF before 20wks wt gain = 298.9g, p=<0.0001). Following adjustment for categories of pre-pregnant BMI a decrease was seen in both the association of complementary food introduction and breastfeeding duration between weight gained from birth to 1yr (CF before 16wks wt gain= 166.7g,p=0.0019; BF before 20wks wt gain= 283g, p=<0.0001). In the final model used, Baker et al. (2004) examined the variables of breastfeeding duration (any) and age at introduction of complementary foods (before 16wks or after 16wks) and weight gained from birth to 1yr, the overall interaction remained significant (p=0.0021). Concluding that early complementary food introduction is associated with increased weight gain; however this was not seen at longer durations of breastfeeding.

The findings of Sloan et al. (2007) who examined weight and weight gain in two cohorts of children, those weaned before 16wks and those weaned after 16wks, to investigate if those children weaned early had greater weight gain than those weaned in line with national guidelines are supportive of those of Baker et al. (2004). Sloan et al. (2007) assessed feeding practices through semi structured interviews of mothers (at infant age of 10mths and 18mths) and weight (kg) was birth weight, weight at 8wks, and 7mths were all obtained from Child Health System and weight was measured at 14mths. Sloan found that 68% (148) of mothers initiated breastfeeding and the mean duration was 20wks and 43% of infants were weaned (introduction of complementary foods) before 16wks and the mean age of weaning was 16.5wks. As breastfeeding was found to be the only variable associated to both weight and the introduction of solids this was controlled for in the linear models.

Mean z-scores (and standard deviations) for weight and weight gain were calculated. Those infants who were weaned early did not have significantly different birth weight scores (p=0.150) or 8wks weight (p=0.555). However, infants weaned early were found to have higher 7mth z-score (p=<0.005) and 14mth z-score (p=0.004) and faster rates of weight gain between 8wks and 14mths (p=0.003). This significant effect was still seen following controlling for breastfeeding; 7mth weight z-scores (p=0.046) and 14mth weight z-score (p=0.035) and weight gain between 8 weeks and 14mths z-score (p=0.029) (Sloan et al. (2007)).

Interestingly, the characteristics of those mothers who introduced complementary foods early (before 16wks) are similar in both studies (Baker et al. (2004), Sloan et al. (2007)) and are as follows: mothers breastfed for shorter periods of time, prepregnant maternal BMI was higher, mother smoked pre pregnancy, were younger and had lower educational attainment and lower SES.

Griffiths, Smeeth, Sherburne Hawkins, Cole and Dezateux (2009) conducted the largest study in this review with a sample size of 10,533 three yr old children from across the UK. Griffiths et al. (2009) discussed the limitations of previous studies being the lack of appropriate adjustment for confounding factors (adjusted confounding factors can be seen in Appendix C1).

As with the previous studies Griffiths et al. (2009) also considered the impact of breastfeeding but the results presented here will concentrate on those related to the introduction of complementary foods. The study design was similar to those already mentioned and consisted of structured interviews at 9mths and 3yrs (which covered feeding practices, family characteristics, confounding factors etc) and weight and height measurements at 9mths and 3yrs, birth weight was reported and converted to z-scores based on 1990 UK growth reference charts. Conditional weight gain was associated with the age at which solids were introduced ($p=<0.001$) and was still significant following adjustment for confounding factors ($p=0.005$), however, when adjusted for height this association was no longer seen. Griffiths et al. (2009) suggested that infants weaned early (before 16wks) were heavier but not necessarily fatter at 3yrs of age. As with all studies there are limitations with this study as both birth weight and feeding behaviour were obtained retrospectively so recall bias may exist.

5.2.2 Age of Weaning and Overweight/ Obesity in Childhood

Reilly et al. (2005) undertook a prospective cohort study in the UK with the aim of investigating the risk factors in early life for obesity in children in the UK. This study was considered to be representative of the population. Reilly et al. (2005) examined the effect of 25 alleged risk factors for childhood obesity in a random sample of 8234 (5493 children had full data and were used in the study) children from the UK aged from 4mths to 5yrs. As with the previous study by Baker et al. (2004), Reilly et al. (2007) adjusted for confounding factors such as SES, gender and food group variables but unlike Baker et al. (2006) found no association between the timing of the introduction of complementary feeding and obesity at age 7yrs ($p=0.296$).

However, Reilly et al. (2007) did find that in a subsample of subjects weight gain within the first year of life (per 100g increase) was an independent risk factor for obesity at age 7yrs (OR: 1.06, 1.02 to 1.10; p= 0.003).

A subsequent study by Burdette, Whitaker, Hall & Daniels (2006) examined the effect of adiposity at age 5yrs and the relationship between breastfeeding and the timing of the introduction of complementary foods. Unlike the previous studies Burdette et al. (2006) used DEXA to measure adiposity, which is considered to be the most accurate measure of adiposity in children as it enables the assessment of body fatness, lean body mass etc as these vary between gender and ethnic group (as previously discussed in Chapter 2). This study also included participants who were black, whereas this was not the case in the other studies mentioned thus far. However, Burdette states that *"there are no well established reference data from which to identify a cut-off for overweight or obesity in children on the basis of body composition from DEXA scans'.* They therefore based their classification on previous studies for cardiovascular risk factors, 'high adiposity' (based on sex specific highest quartiles) if they had a body fat percentage (BF%) of more than 29% for females and more than 24% for males.

Similar study measures were used as with previous studies (with the exception of DEXA scan) including questionnaire based interviews to assess variables, food based questionnaires and weight and height measurements taken using standardised protocol and percentile z scores being calculated.

For those participants who had the DEXA scan at age 5yrs they were significantly more likely to have been breastfed than those who did not (74% and 56% respectively; p=0.007). Fifty percent of mothers followed the American Academy of Paediatrics guidelines, which recommend introducing complementary foods before four months. Burdette et al. (2006) also found that those women who breastfed (compared with those who did not) were significantly more likely to introduce complementary foods later (p=0.0001); thus supporting the findings of Baker et al. (2004)**.**

With respect to body composition and anthropometric measurements examined, as already indicated, fat mass (FM) was significantly lower in black children than white children (4.19kg +/- 0.18kg and 4.64kg +/- 0.09kg respectively, p=0.03), however no difference was seen in body weight BMI z scores.

When considering the introduction of complementary foods and adiposity Burdette et al. (2006) found that fat mass did not differ significantly between those children introduced to complementary foods early (before 16wks) or after 16wks (4.49kg +/- 0.12kg and 4.63kg +/- 0.12kg respectively, p=0.42). Burdette et al. (2006) pointed out that their sample size was rather small and when compared to other studies which have considered BMI, the study lacked the power to determine statistically significant difference in adiposity using DEXA; therefore, it is difficult to apply these findings to other populations. Recommendations from this study are to have larger sample sizes, using DEXA and controlling for confounding factors.

A later study by Robinson et al. (2009) also used DEXA to measure body composition at age 4yrs to examine the relationship between variations in both milk feeding and the weaning diet on adiposity at age 4yrs. Whereas Burdette et al. (2006) graded adiposity in terms of ‘high adiposity’ (as mentioned previously) Robinson et al. (2009) looked at the variance in body composition and BMI (based on IOTF definitions) so it is not possible to directly compare these results. However, Robinson et al. (2009) findings do support those of the previous study (Burdette et al. (2007)), but only a weak association was seen between fat mass at age 4yrs and the age of introduction of solid foods (p=0.034) and this association was no longer seen after adjusting for confounding factors. They also found that neither BMI, fat mass index, lean mass and lean mass index were related to introduction of solids, but this data was not shown. Robinson et al. (2009) also examined the nutritional composition of the weaning diet based on infant feeding guideline scores which will be discussed in section 5.3.2.

Balaban, Motta & Silva (2010) findings support those already discussed. Univariate analysis showed an association between the age of introduction of complementary foods and overweight; however following multivariate analysis this association could no longer be seen. Balaban et al. (2010) undertook a case control study of 366 children aged 2yrs to 6yrs from three cities in South America. The main objective was to investigate if early weaning could be considered as a risk factor for overweight in preschool children. The case group was comprised of overweight children (using Centre for Disease Control, 2000 definitions BMI equal to or >85th percentile) and the control were non overweight. Children who had received exclusive or predominant breastfeeding for less than 16wks (introduced to complementary foods >16wks) had a greater risk of overweight than those who received exclusive breast or predominant breastfeeding for more than 16wks (OR=1.69; 95% CI: 1.10-2.60, p=0.02). Following multivariate analysis this significance was no longer seen (OR= 1.42; 95% CI: 0.86-2.34, p=0.17).

In conclusion, Balaban et al. (2010) found that maternal overweight, birth weight, and sedentary behaviour are important risk factors which require consideration; these were also identified by Reilly et al. (2005).

The most recent study to examine the timing of the introduction of complementary foods and the risk of obesity in pre-school aged children is by Huh, Rifas-Shipman, Traveras, Oken and Gillman (2011). Huh et al. (2011) studied 84 children in the Project Viva, prospective birth cohort study. The timing of solid introduction was assessed via a questionnaire based on the introduction of 10 foods or food groups. Categories were then assigned to the groups of up to 4mths, 4mths to 5mths or 6mths or older. Anthropometric measurements taken (by a trained professional) were height, weight and BMI percentile (based on US reference data- CDC, 2000) and z-scores calculated; birth weight and weight at 4mths were taken from medical records and age and gender specific weight for ages z-scores were calculated. Weight gain from 0 to 4mths was calculated using a subtraction calculation. Unlike Baker et al. (2004), Huh et al. (2011) did not exclude subjects that had never breastfed; these subjects were included into the formula feeding sample. Huh et al. (2011) found that 33% of formula fed infants were introduced complementary foods before 4mths (16wks) compared to 8% of breastfed infants; and 9% of formula fed infants were introduced to complementary foods 6mths or later compared to 17% of those breastfed (p=<0.0001). These finding are consistent to those of previous studies discussed. Suggesting that the breastfed infants are more likely to be introduced to complementary foods later than those never breastfed, breastfed for less than 4wks or formula fed.

Seven percent of breastfed infants were found to be obese at 3yrs of age (BMI>95th percentile) compared to 13% of formula fed infants and the mean BMI z-scores and the sum of skinfold thickness was also higher in formula fed infants. Following bivariate analysis, the relationship between timing of solid food introduction with obesity differed according to breastfeeding status (this can be seen in Figure 5) (Huh et al. 2011).

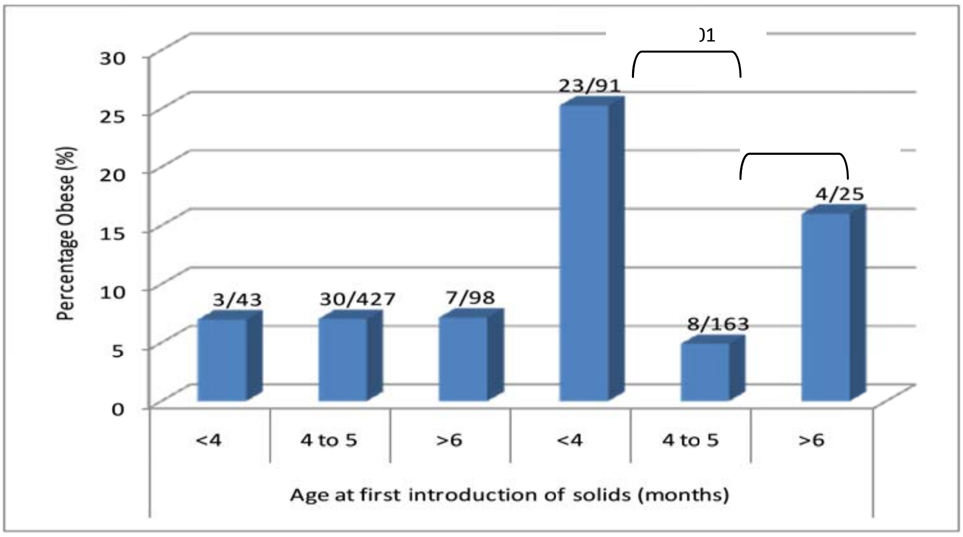

Figure 5: Association between the timing of solid food introduction and obesity at 3years of age (BMI>95th percentile) according to breastfeeding status (recreated from Huh et al. (2011))

Breastfed infants who received solid foods between the age of 4mths and 5mths compared to those fed before 4mths did not have an increase risk of obesity at age 3yrs (OR:1.0 (95% CI: 0.3-3.3- unadjusted), following adjustment for weight for age z scores from 0 to 4mths this did not change. However, formula fed infants who received solids before 4mths compared to those fed 4mths to 5mths had a six fold increase in the odds of obesity at 3yrs (OR:6.3, 95% CI 2.3-16.9- adjusted). For those infants formula fed after 6mths a 3.6 fold increase in the odds of obesity after adjustment for covariates but wide CI existed (95%, 0.8-16.3) (Huh et al. (2011)).

Huh et al. (2011) findings regarding the introduction of solids on BMI in early childhood differ to those of Reilly et al. (2005), Burdette (2006), Robinson et al. (2009), and Balaban et al. (2010) who found no relationship between introduction of solids and BMI. This could be due to the differences in the ages considered in the studies (4yrs, 6yrs, and 7yrs), definitions used, in accurate recall regarding weight, timing of complementary foods etc, differing adjustments for confounding factors.

5.3 Effect of the Nutritional Composition of the Weaning Diet on Weight Gain and Overweight and Obesity in Children

This section is concerned with the review and analysis of studies or aspects of studies which have investigated the effects of the nutritional composition of the weaning diet and the rate of weight gain and/ or overweight/ obesity in children. The nutritional composition in the main refers to the macronutrient content of the weaning diet, however some studies have considered other parameters such as eating in the absence of hunger and dinner test meals, these additional comparisons will be discussed within the following sections.

The rationale for considering the effect of the nutritional composition of the diet in early infancy is due to a body of evidence suggesting an association with different macronutrients on weight gain and or overweight/ obesity in childhood. As with section 5.2, the weight gain and weight parameters include skinfold thickness measurements and DEXA.

Table 6, illustrates the study design, subjects, classification of overweight/ obesity used, measurements taken, the nutritional composition of the weaning diet (energy, dietary fat, dietary carbohydrate, and dietary protein, all as % of total energy intake) main outcomes and findings on the age of weaning and weight gain or overweight/ obesity in childhood. Full details can be seen in Appendix C2.

Table 6: Nutritional Composition of the Weaning Diet- Effect on Weight Gain and/ or Overweight/ Obesity in Childhood

Author & Date	Location	Study Design	Down's Black Score	Subjects (n)[a]	Overweight/ Obesity Classification [b]	Measurements [c]	Total Energy Intake (KJ/d) [d]	Dietary Fat (% of energy)[d]	Dietary Carbohydrate (% of energy) [d]	Dietary Protein (% of energy) [d]	Findings [e]
Scaglioni et al. 2000	Italy	Cohort (Longitudinal)	21	147 children 84 males; 80 females. Aged 5yrs	Overweight: 90th centile (age and sex adjusted Rolland-Cachera curves)	Weight; Length.	p=0.663	p=0.728	p=0.031	p=0.024	Parental overweight is a major risk factor for childhood overweight in the first years of life, but an early high protein intake may also influence the development of adiposity.
Gunnarsdottir et al. 2003	Iceland	Cohort (Longitudinal)	21	90 41 males; 49 females. Aged 6yrs	IOTF definitions based on BMI at 18yr	Birth Weight (kg);	not significant (p value not given)	not significant (p value not given)	not significant (p value not given)	Boys 2mth- p= 0.003 4mth-p=0.027 6mth-not significant 9mth- p=<0.001 12mth- p=<0.001 Girls no significant difference at any age	Rapid growth during the first year of life is associated with increased BMI at the age of 6yrs in both genders. In boys, high intake of protein in infancy could also contribute to childhood obesity.
Hoppe et al. 2004	Denmark	Observational Cohort	22	143 children 63 males; 80 females. Aged 10yrs	IOTF definitions based on BMI at 18yr	Weight; Length; triceps and sub scapular thickness; Duel x ray absorptiometry scanning (DXA) at 10yrs	3088kJ/d = 349kJ/kg body wt	89g/d	286g/d	2.7g/d= 0.9-4.2g/kg body wt. P=0.007	1% increase in protein intake at 9mths is associated with an increased weight at age 10yrs of approximately 0.44kg and an increase in length at age 10yrs of approximately 0.51cm (p=0.009).

Table 6: Nutritional Composition of the Weaning Diet- Effect on Weight Gain and/ or Overweight/ Obesity in Childhood continued

Author	Location	Study Design	Down's Black Score	Subjects (n)[a]	Overweight/ Obesity Classification [b]	Measurements [c]	Total Energy Intake (KJ/d) [d]	Dietary Fat (% of energy)[d]	Dietary Carbohydrate (% of energy) [d]	Dietary Protein (% of energy) [d]	Findings [f]
Günther et al. 2007	Germany	Longitudinal cohort	23	203 children 104males; 99 females. Aged: birth to age 7yrs	IOTF definitions based on BMI at 18yr	Birth Weight (kg) Weight (kg) Height (cm) Scapular and Triceps thickness	n/a	n/a	n/a	p=0.02	High protein intake during the period of complementary feeding and the transition to the family diet are associated with an unfavourable body composition at age 7yrs.
Butte, N.F. 2009	USA	Cohort	14	1030 Hispanic Children (gender not broken down) Aged 4-19	Overweight- >95 percentile Centres for Disease Control (CDC) BMI 2000	Birth Weight (kg)	p= 0.003	p=0.11	p=0.03	p=0.14	Age of introduction of solids was not associated with the risk of obesity. Total energy intake, ad labium energy intake at dinner and amount of energy consumed in absence of hunger associated with increase risk of obesity.

a: Subject (males/ females and author classification if appropriate).
b: Classification of overweight/ obesity used in relevant studies.
c: Refers to the key measurements taken as part of the study, for example, weight, weight gain, DEXA scan.
d: States the key findings for the study which are significant in relation to the macronutrient (p= <0.05).
e: Describes the key findings of the study.

5.3.1 Effect of Nutritional Composition of the Weaning Diet on Overweight/ Obesity in Childhood

For the purpose of this section the weaning diet refers to the food consumed between the first introduction of complementary foods and when the infant reaches 1yr of age. As with section 5.2 the results of the review will be presented chronologically by date of study.

The earliest study reviewed in this section is by Scaglioni, Agostoni, De Notaris, Radaelli, Radice, Valenti, Giovannini & Riva (2000). The aim of this study was to examine the influence of macronutrient intake in early life on the development of overweight in children. To do this Scaglioni et al. (2000) completed a longitudinal study with 147 healthy children (all Caucasian), followed up from birth to 5yrs of age. Anthropometric measurements and nutritional assessment took place at birth, 1yr and 5yrs. Age adjusted food questionnaires and 24hr food recall diaries completed by trained professionals were used to assess nutritional intake. Weight and length/ height were completed using age appropriate techniques. Scaglioni et al. (2000) found that during the period of the study the percentage of overweight subjects increased from 10.9% at age 1yr to 23.1% at age 5yrs (p=<0.001), no significant difference was seen between genders (p=0.32). However, correlations were seen between BMI at age 1yrs and at 5yrs (r=0.35, p=<0.0001) and maternal and paternal BMI (r=0.21, p=0.01 and r=0.35, p=<0.0001, respectively) and that those children overweight at age 5yrs were more likely to have parents who were also overweight. Children were separated into two groups those overweight (BMI>90th percentile) or not overweight (BMI<90th percentile). Children who were overweight at 5yrs consumed significantly higher protein as a percentage of total energy intake (p=0.024) and less carbohydrate as a percentage of energy (p=0.031) than non overweight children.

When considering macronutrient intake and overweight at age 5yrs, only protein as a percentage of energy (and following adjustment for parental BMI), was considered to be significant (p=0.05). Similar findings were seen when considering the non overweight sub-set only, protein intake p=0.03, as % total energy intake. It is suggested that protein intake in early life increases the risk of obesity due to high protein intake stimulating the secretion of insulin like growth factor 1 (IGT-1) and thereby protein synthesis and cell proliferation (Rolland-Cachera, Deheeger, Arout & Bellisle, 1995). Scaglioni et al. (2000) did raise the concern that 51% of the parents were classified as overweight, and therefore genetic factors could be implicated, even though within the analysis parental BMI and weight were adjusted for.

A later study by Gunnarsdottir & Thorsdottir (2003), attempted to limit bias of recall when reporting food intake and completed monthly weighed food diaries during infancy; with weighed food diaries being completed at 2mths, 6mths and 12mths. Anthropometric measurements were taken at birth (however, the birth weights were obtained retrospectively from infant records), 12mths and 6yrs. They found that boys in the highest quartile of protein intake (as a percentage of energy) at 9mths to12mths had significantly higher BMI at 6yrs than those in the lowest and second lowest quartile of protein intake (% of energy) (17.8kg/m^2 +/- 2.4kg/m^2; 15.3kg/m^2 +/- -0.8kg/m^2 and 15.5kg/m^2 +/- 1kg/m^2, respectively). No significance was seen in girls. Gunnarsdottir & Thorsdottir (2003) suggests that the difference in the effect of protein (%total energy intake) between boys and girls in this cohort could be due to the differences in growth patterns between genders, which could reflect the effects of early sex hormone production in males or due to endocrinological differences. Gunnearsdottir & Thorsdottir (2003) also found that rapid growth during the first year of life is associated with increased BMI at the age of 6yrs in both boys and girls (boys= 2.9 +/- 1.0, p=0.008, girls= 2.0 +/-0.9, p=0.032).

5.3.2 Effect of the Nutritional Composition of the Weaning Diet on Weight Gain

The initial study examining the relationship between nutritional intake and weight gain was Hoppe, Molgaard, Thomsen, Juul and Michaelsen (2004). They investigated the association between protein intake in infancy and body size and composition in late childhood. Hoppe et al. (2004) states that protein intake of infants increases by three to four times during weaning stage, (from approximately 1g/kg body wt). To investigate the relationship they observed 142 healthy Danish children and assessed nutritional intake, puberty assessment, blood analysis (IGF-1), anthropometrics (including using skinfold thickness and DEXA scanning) at age 9mth and 10yrs.

The median daily protein intake was 2.7g/kg body weight (13.3% of energy) (range: 0.9-4.2g/kg body weight (6.5-20% of energy).Total daily protein intake and percentage of energy from protein were significantly correlated with body size (weight and length; $p \leq 0.0001$) but not with adiposity (via skinfold thickness) at 9mths ($p=0.464$). Protein intake at 9mths was positively correlated with percentage of energy from protein at age 10yrs ($r=0.28$, $p=0.01$) which suggests that high intakes of protein continue through childhood and are due to food preferences of the family and child. This pattern was also seen in terms of weight and length or height ($r=0.35$, $p=<0.0001$ and $r=0.53$, $p=<0.0001$ respectively) and IGF-I ($r=0.27$, $p=0.03$). Additionally, Hoppe et al. (2004) showed that a 1% increase in protein intake at 9mths is associated with an increased weight at age 10yrs of approximately 0.44kg and increased length at age 10yrs of approximately 0.51cm ($p=0.009$). However, protein intake at 9mth was not significantly associated with percentage body fat at 10yrs (p value not given).

Hoppe et al. (2004) concluded that *'high protein intake stimulates early growth. Possibly explaining the association between early protein intake and body size at 10yrs, however, the continuous effect of protein on growth during childhood cannot be excluded. Protein intake was not associated with any measure of body fat at age 10yrs'.* The main limitations with this study were the small number of overweight children and none of whom were obese, and the protein intake of the study subjects; as in previous studies mentioned by Hoppe et al. (2004) subjects had consumed up to 4-5% higher.

These findings are challenged by those of Gunther, Buyken and Kroke (2007) who found no association between protein intake at 6mths with BMI and body composition at age 7yrs. The Dortmund Nutritional Anthropometric

Longitudinally Designed Study (DONALD Study) (Gunther et al. (2007)) assessed dietary intake at 6mths, 12mths and 18mths to 24mths and anthropometric measurements of birth weight (kg), weight (kg), height (cm) and scapular and triceps thickness and calculated BMI (sex dependant scores given). Gunther et al. (2007) was the first study to consider protein intake across infancy and into early childhood, but for the purpose of this review we are only interested in the findings of protein intake during the weaning phase. During the infancy period (6mth to12mth) of the study protein intakes were categorised as ‘low-low’(LL), ‘low-high’ (LH), ‘high-low’ (HL) and ‘high-high’ (HH). It was found that protein intakes differed from between the low and high intake groups at 6mths (7-8% of energy compared to 12%) and 12mths (11-12% of energy compared to 14-15%) but no variation at later ages, suggesting no tracking of protein intake which was previously put forward by Hoppe et al. (2004). When comparing the high and low protein groups and BMI SD scores (SDS) found no association at 6mth or 12mth (p=0.51 and p=0.76, respectively). However, a high protein intake at 12mth was associated with a higher BMI SDS at age 7yrs (p=0.02), similar results seen for %BF (p=<0.0001). The DONALD Study (Gunther et al. 2007) suggests an association between early protein intakes and later BMI, and percentage body fat but not height. Gunther et al. (2007) discuss the limitations of the study as being the limited transferability of equations to the population due to the susceptibility of errors in measurement, small sample size, and that not all protein combinations were assessed separately. In addition the sample size was not representative of the whole population, and the range of protein intakes as this was not a large as in other studies.

The penultimate study completed by Butte et al. (2009) was designed to identify genetic and environmental factors affecting obesity and its co-morbidities in 1030 Hispanic children aged between 4yrs and 19yrs.
To assess nutritional intake two 24hr food record charts were used. Total energy intake (p=0.003) was positively associated with risk of childhood obesity as was ad lib energy intake at dinner and amount of energy consumed in the absence of hunger. However, the age of introduction of solids was not related to the risk of obesity. This study was the lowest scoring in terms of Downs and Black Assessment (scored 14). Information was missing or not clearly presented such as confounding factors, the difference between those populations who were recruited and did or did not participate in the study and the techniques age at measurements and place where measurements took place or the differences between those lost to follow ups and those who continued in the study were not identified.

The final study by Robinson et al. (2009) has already been discussed in section 5.2.2. Unlike the other studies in this section of the review, Robinson et al. (2009) used a general measure of food intake based on dietary guidelines rather than a breakdown of macronutrients (e.g. g protein). To limit reporting bias all interviews were undertaken by a trained nurse at 6mth and 12mth, the study also used DEXA scan to measure body composition (considered to be the gold standard) and adjusted for a range of confounding factors (Appendix C1). No association between infant dietary guideline pattern scores at 12mths and body composition at age 4yrs; however, lean mass and lean mass index were positively associated with the infant guideline scores (results can be seen in Table 7).

Table 7: Association between infant guideline scores at 12mths and body composition at age 4yrs (taken from Robinson et al.(2009))

Infant Guideline Score	Mean (95% CI)				
	BMI (kg/m^2)[b]	Lean Mass (kg)	Lean Mass Index (kg/m^2)[b]	Fat Mass (kg)[b]	Fat Mass Index (kg/m^2)[b]
<- 0.68	15.9 (15.6-16.1)	12.0 (11.7-12.4)	11.7 (11.5-11.9)	4.5 (4.3-4.7)	4.3 (4.1-4.4)
<-0.68 to 0	16.1 (15.8-16.3)	12.3 (12.1-12.6)	11.8 (11.6-11.9)	4.7 (4.5-4.9)	4.3 (4.2-4.5)
0 to 0.68	16.2 (16.0-16.5)	12.7 (12.4-12.9)	11.9 (11.8-12.0)	4.7 (4.5-4.9)	4.3 (4.2-4.5)
<0.68	16.1 (15.8-16.3)	12.6 (12.3-12.9)	11.9 (11.8-12.1)	4.5 (4.3-4.6)	4.1 (4.0-4.3)
p for trend[c]	0.205	0.001	0.011	0.609	0.166
p for trend (adjusted)[d]	0.102	0.004	0.004	0.781	0.488

a- all values were adjusted for sex

b- Geometric means

c- From linear regression analysis

d- Adjusted for maternal age, BMI, height, education, social class, smoking in late pregnancy, infant birth weight, and age of introduction of solid foods

Infant feeding guideline scores were calculated using the coefficients for each food group and the infants reported frequency of consumption of that group; these values were then summed to provide a single score for the infant which was used to indicate their compliance with the pattern (Robinson et al. (2009)). Infants who were weaned in accordance with these guidelines had a higher lean mass (p=0.003) and lean mass index (p=0.005) at age 4yrs (this can be seen in Figure 6).

Figure 6: Body composition at age 4yrs and association with infant guidelines (taken from Robinson et al. 2009)

Robinson et al. (2009) concludes that *'adherence to current recommendations to breastfeed and to provide a weaning diet based on fruit, vegetables and home prepared foods is associated with a higher lean mass and lower fat mass at age 4'.*

CHAPTER 6

DISCUSSION

The effects of both the age at the introduction of complementary feeding and of the nutritional composition of the diet in infancy (0mth to 1yr) and their relationship with weight gain and or overweight/ obesity in childhood have been examined by a number of studies. The rationale for examining these effects are that both weight gain during early infancy and the age of weaning have been identified as being possible risk factors for overweight and obesity in childhood.

All the studies are observational in design and are therefore limited by methodology, sample sizes and not being representative of populations, preconceived ideas, some studies used retrospective data collection (data dredging) and not adjusting appropriately for confounding factors.

Different assessments and criteria were used to measure adiposity and BMI and meta analysis was not undertaken on the studies reviewed. However, the results compiled are based on interpretation of the results of the studies and these results along with the discussion will determine if any relationship can be seen. The discussion will be presented (as in previous sections) as follows:

- Age of introduction of complementary foods and effect of weight gain;
- Age of introduction of complementary foods and effect on overweight/ obesity;
- Nutritional composition of the diet from 0mth to 1yr on weight gain;

- Nutritional composition of the diet from 0mth to 1yr on overweight/ obesity;
- Additional findings of interest, finally
- Limitations of the review.

6.1 Age at introduction of complementary foods and effect on weight gain

Three studies considered this area and the number of subjects in these studies ranged from 234 children to 10,553 children and varied in the quality assessment. With respect to the quality assessment two of the studies scored 17 and 18 (Baker et al. (2004) and Sloan et al. (2007) whereas the study by Griffiths et al. (2009)) scored 21. The main difference in the assessments was due to the population size, not fully reporting the interventions of interest or when the study population were selected or if data was obtained retrospectively. In terms of adjusting for confounding factors which is a know limitation with observational studies, all three studies did report to undertake both univariate and multivariate analysis and controlling for confounding factors was observed.

All of the studies examining the relationship between age at introduction of complementary feeding and effect of weight gain found those children who were weaned early (less than 16wks) gained more weight than those not weaned earlier than 16wks. These findings were of greater significance in those infants who were not breastfed or breastfed for less than 4wks. It could be hypothesised that this could be due to the higher protein intakes increasing the release of Insulin Growth Factor 1 (IGF-1).

One study did exclude mother infant pairs that had never breastfed (Baker et al. (2004)) (65 people) whereas the other two studies included these subjects (Sloan et al. (2007); Griffiths et al. (2009)). It was considered by Baker et al. (2004) that this would not significantly affect the results as the number of non breastfed infants accounted for less than 1% of population and had unusual circumstances. All studies show that following adjustment for confounding factors significant difference was still seen. When considering these results and their interpretation for the population level the only study to be a multicentre and have a significant sample size was that of Griffiths et al. (2007), however they did not directly report it's representativeness to the population within this study.

These findings are of interest when considering 51% of the of infants in the UK are introduced complementary foods before 16wks (Bolling et al. (2007)) and that earlier evidence suggests that weight gain in early infancy (by age 1yr) is often associated with future weight gain (Ong et al. (2006); Reilly et al. (2007)).

6.2 Age of introduction of complementary foods and effect on overweight/ obesity

Five studies examined the relationship between age of complementary food introduction and adiposity/ overweight/ obesity in childhood, of which only one study found a significant relationship (Huh et al. (2010)). Huh et al. (2010) found that formula fed infants had a 6 fold increase in odds of obesity at age 3yrs if commenced on complementary foods before 16wks, there was no association with those children who were breastfed. Assessments for quality scores were similar in the five studies, scoring either 19 or 20, therefore no variation in terms of quality existed between those studies found to have a significant or not to have a significant difference.

The possible reasons for the difference in the findings of Huh et al. (2010) compared to those findings no significant relationship could be due to the differences in the ages considered in the studies (4yrs, 6yrs, and 7yrs), definitions used, bias in recall regarding weight and timing of complementary foods etc. Huh et al. (2006) assessed diet at 6mth whereas Burdette et al. (2006) used a recall based dietary assessment when the infant was 3yrs, Balaban et al. (2010) used a similar approach to Burdette et al. (2006) but recall was at varying ages from 2yrs to 6yrs, Robinson et al. (2009) assessed intake 6mth and 12mth but used a different assessment tool to Huh et al. (2010). Finally, as previously mentioned differing adjustments for confounding factors would lead to differences in significance.

6.3 Nutritional composition of the diet from 0mth to 1yr on weight gain and of overweight/ obesity in childhood

Findings relating to nutritional intake during the first year of life and its relationship with weight gain and overweight/ obesity status were more convincing than that for age of introduction of solids as four of the five studies reviewed showed a significant association. The most significant effect being that of protein as a percentage of energy intake. Scaglioni et al. (2000) observed that children who were overweight at 5yrs consumed significantly higher protein as a percentage of total energy intake ($p=0.024$) and less carbohydrate as a percentage of energy ($p=0.031$) than non overweight children. Gunnardottir et al. (2003) showed that rapid growth during the first year of life is associated with increased BMI at the age of 6yrs in both boys and girls (boys= 2.9 +/- 1.0, $p=0.008$, girls= 2.0 +/-0.9, $p=0.032$). Hoppe et al. (2004) found that protein intake was associated with increase weight gain and length but not adiposity at 9mths ($p=<0.0001$ and $p=0.464$ respectively), as well as finding that a 1% increase in protein intake at 9mths is associated with both an increase in weight of 0.44kg and 0.51cm in length at age 10yrs ($p=0.009$). The most recent study by Gunther et al. (2007) who focussed solely on protein intake and BMI supported these findings, showing high protein intake at 9mths is associated with higher BMI and percentage body fat at 7yrs ($p=0.02$ and $p=0.0001$, respectively).

Hoppe et al. (2004) used DEXA as its method of analysis and is considered to be most accurate in terms of its assessment of body composition whereas the other studies used height and weight z scores and skinfold thickness assessments, the possible errors associated with these assessments (e.g. incorrect methodologies used, competence of person using callipers etc) need to be considered in interpreting these findings. Hoppe et al. (2004) was the only study that measured additional markers of serum urea nitrogen (SUN) and IGF-1. SUN is considered to be a marker of recent protein intake and was associated with reported protein intake at both 9mths and 10yrs of age. IGF-I concentrations at 9mths were associated with protein intake and SUN concentrations suggesting that a high protein intake increases IGF-I concentrations in healthy infants. IGF-I has previously been associated with obesity (Rolland-Cachera et al. (1995)).

All studies had similar assessments of quality ranging from 21 to 23. The variations between the studies were regarding the reporting of confounding factors and the representativeness of the populations.

6.4 Additional findings of interest

Throughout the review researchers discussed the characteristics of mothers who introduced complementary foods prior to 16wks. The characteristics of those mothers are as follows:

- Breastfed for shorter periods of time;
- Higher prepregnant maternal BMI;
- Smoked pre pregnancy;
- Younger age;
- Lower educational attainment and
- Lower SES.

This is supportive of the findings of Scott, Binns, Graham & Oddy (2009) who examined the maternal and infant characteristics associated with the timing of the introduction of solids in 519 participants in the Perth Infant Feeding Study. Scott et al. (2009) found the independent predictors of early introduction of complementary foods were young maternal age, maternal smoking pre pregnancy and not solely breastfeeding at 4wks (introduced formula feeding).

These additional findings could be used to inform policy makers and health professionals working with new mothers and infants to target the population appropriately and therefore tailor support and educate people on appropriately feeding their infant and infant nutrition.

6.5 Limitations

The main limitation of this systematic review was the availability of the original research and in obtaining the relevant articles in line with the methodology and protocols (inclusion and exclusion criteria) set out in Chapter 4. The studies included in this review were not representative of the whole population as they tended not to include individuals from ethnic groups, therefore all findings should be considered with care when being generalised to the whole population.

The different methods off assessing adiposity and different cut offs for BMI limits, as well as not undertaking a meta analysis limits the ability to directly compare studies which also limits the findings of this review.

CHAPTER 7

CONCLUSIONS AND RECOMMENDATIONS

Overweight and obesity in childhood is increasing worldwide and with it comes additional cost not only to the infant in terms of health but also to the economy as a whole. It is paramount that we identify risk factors and appropriate mechanisms for reducing identified risk factors in the future so as to stem the rising epidemic of childhood obesity.

This review shows that the evidence for the impact of early weaning on adiposity levels, overweight and/ or obesity remains inconsistent. The findings do suggest that there is no relationship between adiposity and BMI in childhood with early weaning practices (only one study found significant relationship).

However, the introduction of complementary foods before 16wks was shown to lead to greater weight gain in early childhood, independent of other confounding factors, especially in those infants who are fed formula food or breastfed for less than 4wks, which in turn could lead to overweight and obesity in later childhood. High protein intake (as percentage of energy) is strongly suggested to influence weight gain during infancy and BMI in early childhood.

Recommendations for Policy/ Health Care Professionals

The identification of the characteristics of those mothers who wean their infants early could be incorporated into policy as it provides evidence of where health professionals should focus their resources. It could be concluded that health professionals should recommend the following:

- Children are weaned in line with existing policy and this should commence from 6mths of age (breastfeeding solely up until this time and maintaining breastfeeding particularly during the early stages of weaning);
- The diet should be based on carbohydrates, fruit and vegetables and moderate intakes of protein, limiting the intake of processed, salty and sugary foods;
- Foods such as honey and whole nuts should still be avoided until the age of 5yrs;
- Targeted health education programmes should be developed for both prospective and new parents who are overweight/ obese and smoke and for those younger parents to provide them with the knowledge to make healthier choices for themselves and their child/ children.

Recommendations for Future Research

It is clear that further research is required in this field; it is recommended that future research should include/ be:

- Larger population sizes;
- Representative of the population and should include mixed ethnicities and wider socio-economic groups (this was one of the main limitations of most of studies analysed);
- As well as using weight (g or kg) to assess weight gain and weight changes studies should also use high quality methods for measuring

adiposity (such as DEXA) rather than BMI or skinfold thickness due to the error associated and the difficulty in comparing these measurements between studies;

- Use of weighed food and fluid intakes (before and after meals) to obtain accurate food and fluid consumption to be completed by parents/ carers, to enable accurate analysis of nutritional composition of the diet;
- A future UK based study could be considered which would look at the relationship between the nutritional intake and weight (kg) and length (cm) during the first year of life and weight (kg), height (cm) and BMI (kg/m^2) at reception and Year 6 (possibly also using DEXA with a sub sample of the population).

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Appendix A: Adapted Down's & Black Assessment Tool (1998)

Down's & Black Assessment Questions			Score Available	
Retporting	1	Is the hypothesis/ aim/ objective clearly described	Yes	1
			No	0
	2	Are the main outcomes to be measured clearly described in the introduction or methods sections	Yes	1
			No	0
	3	Are the characteristics of the patients included in the study clearly described	Yes	1
			No	0
	4	Are the intervention of interest clearly described	Yes	1
			No	0
	5	Are the distributions of principal confounders in each group of subjects to be compared clearly described	Yes	2
			Partially	1
			No	0
	6	Are the main findings of the study clearly described	Yes	1
			No	0
	7	Does the study provide estimates of random variability in the data for the main outcomes	Yes	1
			No	0
	8	Have all important adverse events that may be a consequence of the intervention been reported	Yes	1
			No	0
	9	Have the characteristics of patients lost to follow up been described	Yes	1
			No	0
	10	Have actual probability values been reported (0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001	Yes	1
			No	0
External Validity	11	were the subjects asked to participate in the study representative of the entire population from which the study subjects were recruited	Yes	1
			No	0
			Unable to Determine	0
	12	Were those subjects who were prepared to participate representative of the entire population from which they were recruited	Yes	1
			No	0
			Unable to Determine	0
	13	Were staff, placed and facilities where the patients were treated, representative of the treatment the majority of patients received	Yes	1
			No	0
			Unable to Determine	0
Internal Validitiy- Bias	14	Was an attempt made to blind the subjects to the intervention they received	Yes	1
			No	0
			Unable to Determine	0
	15	Was an attempt made to blind those measuring the main outcomes of the intervention	Yes	1
			No	0
			Unable to Determine	0
	16	If any of the results of the study were based on 'data dredging' was this made clear	Yes	1
			No	0
			Unable to Determine	0
	17	In trials and cohort studies, do the analysis adjust for different lengths of follow up of patients, or in case-control studies, is the time period between the intervention and outcomes the same for cases and controls	Yes	1
			No	0
			Unable to Determine	0
	18	Were the statistical tests used to assess the main outcomes appropriate	Yes	1
			No	0
			Unable to Determine	0
	19	Was compliance with the interventions reliable	Yes	1
			No	0
			Unable to Determine	0
	20	Were the main outcome measures accurate (valid and reliable)	Yes	1
			No	0
			Unable to Determine	0
Internal Validitiy- Confounding	21	Were the patients in different intervention groups (trials and cohort) or were the cases and controls (case control studies) recruited from the same population	Yes	1
			No	0
			Unable to Determine	0
	22	Were study subjects in different intervention groups (trials and cohort) or were the cases and controls (case controls) recruited over the same period of time	Yes	1
			No	0
			Unable to Determine	0
	23	Were study subjects randomised to intervention groups	Yes	1
			No	0
			Unable to Determine	0
	24	Was the randomised intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable	Yes	1
			No	0
			Unable to Determine	0
	25	Was there adequate adjustment for confounding in the analysis from which the main findings were drawn	Yes	1
			No	0
			Unable to Determine	0
	26	Were losses of patients to follow-up taken into account	Yes	1
			No	0
			Unable to Determine	0
Power	27	Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is less than 5%	Yes	1
			No	0
Total Score (max 28)				

Appendix B: Study Summary Sheets

Author (s): Sloan et al. (2007)

Title: Early weaning is related to weight and rate of weight gain in infancy

1. Location and Funding	Queens University Belfast, BT9 1LP
2. Objectives of Study	Compare weight and weight gain in two groups of infants, those weaned early (<16wks) and those weaned at or later than 16wks.
3. Study Design	Cohort
4. Number of and Description of Subjects	234 participants from Eastern Health and Social Care board, Northern Ireland. Of which full data was available for 210 (weight at 14months) and 216 completed feeding visits.
5. Variables Measured	**Weight**- SECA 834 **Demographics**- National statistics socioeconomic classification method; **Weaning practices**- retrospectively when children were 10 and 18mths via semi structured interview.
6. Age at measurement	Birth 8 weeks 7 months 14 months
7. Definition of Obesity	n/a
8. Duration of Study	Not discussed
9. Statistics Analysed	Weight gain z scores- EXCEL algorithm (Cole 1995); One Way ANOVA to compare weight and weight gain z scores; ANOVA, Chi Square & Correlations tested for association between weight, weight gain and possible confounding factors; Analysis of covariance undertaken to control for breastfeeding.
10. Results	Weight & Weight Gain: Mean SD Birth z score 0.13 0.82

	8 weeks 0.25 1.01 7 mths 0.03 1.07 14 mths 0.10 1.06 Weight gain 8wks to 14 mths 0.09 1.15 Infant Feeding: 43% of infants were weaned before 4 months (16wks). Mean age when solids were introduced was 16.5wks, earliest reported introduction 4weeks. Characteristics of 'early weaning group': younger mums, lower educational levels, lower SES, lower annual household income, formula feeding at birth (p=0.004) and shorter duration of breastfeeding (p=<0.0001). Infants weaned before 12 weeks were on average breast fed for less than 12 weeks compared with those for 24weeks. Infant Feeding and Weight Infants weaned early had higher 7mth z score (p=<0.005) and 14mth z score (p=0.004) and faster rates of weight gain between 8 weeks and 14 mths (p=0.003). Infants who were weaned early did not have significantly different birth weight scores (p=0.150) or 8wks weight (p=0.555). Following controlling for breastfeeding as significant effect of early weaning on 7 mth weight z scores (p=0.046) and 14 moth weight z score (p=0.035) and weight gain between 8 weeks and 14 months z score (p=0.029).
11. Conclusions	The timing of the introduction of solid foods to the infants diet has an effect on weight gain. If weaning is related to rapid weight gain, which is linked to obesity, parents need to be encouraged and supported by health visitors and other Health Care Professionals (HCP) to comply with weaning recommendations.
12. Full Reference	Sloan, S., Gildea, A., Stewart, M., Sneddon, H., & Iwaniec, D. 2007. Early Weaning is related to weight and rate of weight gain in infancy. *Child: care, health and development.* 34, 1, 59-64.

Appendix B: Study Summary Sheets continued

Author (s): Burdette et al. (2006)

Title: Breastfeeding, introduction of complementary foods and adiposity at 5 years of age.

1.	Location and Funding	University of Pennsylvania School of Medicine, Mathematica Policy Research, Cincinnati Children's Hospital Medical Centre. Funding: National Institutes for Health
2.	Objectives of Study	Ascertain if adiposity at age 5 is related to breastfeeding, to the timing of introduction of complementary foods during infancy or both.
3.	Study Design	Cohort Study
4.	Number of and Description of Subjects	**313 participants, age 3 years.** 142 white males; 24 black males; 107 white females; 40 black females.
5.	Variables Measured	**Breastfeeding and formula feeding** – mother reported feeding practices in 1st year; **Complementary feeding**- questioned when commenced complementary feeding and sweetened drinks; **Fat Mass**- though Duel Energy X ray Absorptiometry (Hologic 4500, paediatric software); **Height**- using wall mounted stadometer, 602VR Holtonin, UK); **Weight**- using SECA 770; **BMI**- percentile and z score.
6.	Age at measurement	5yrs
7.	Definition of Obesity	85th percentile- overweight; 95th percentile- obese.
8.	Duration of Study	3 years
9.	Statistics Analysed	FM, adjusted for LBM and sex, was used as the primary dependent variable. Adjusted FM, rather than %BF, was selected as the primary measure of adiposity in the analyses involving a continuous

	dependent variable. Chi-square tests were used to evaluate the bivariate relations between the exposures(breastfeeding and introduction of complementary foods) and the covariates. Multivariate linear regression was used to calculate the mean FM, adjusted for covariates, at each level of the given feeding variable. Multivariate regression to evaluate the covariate-adjusted relation between breastfeeding (and introduction of complementary foods) and other secondary dependent variables, such as the percentage of children with high adiposity, BMI *z* score, and percentage of children who were overweight (BMI _ 85th percentile). All analyses were conducted by using SPSS for WINDOWS software (version 12.0; SPSS Inc, Chicago, IL).
10. Results	No statistically significant relationship was seen between adiposity at age 5 as measured by DXA, either breastfeeding or the timing of the introduction of complementary foods during infancy. Even children who were breastfed for >1yr and who were never fed formula had a total fat mass that didn’t differ significantly from that of children who were never breastfed, when adjusted for covariates. However, before adjustment, BMI was used as a surrogate measure of adiposity a protective effect of breastfeeding on later adiposity was seen.
11. Conclusions	No relationship was seen between breastfeeding or the time of the introduction of complementary food and adiposity at age 5.
12. Full Reference	Burdette, H.L., Whitaker, R.C., Hall, W.C., & Daniels, S.R. 2006. Breastfeeding, introduction of complementary foods, and adiposity at 5yr of age. *The American Journal of Clinical Nutrition.* 83, 550-558.

Appendix B: Study Summary Sheets continued

Author (s): Robinson et al. (2009)

Title: Variations in Infant Feeding Practice are Associated with Body Composition in Childhood: a Prospective Cohort Study

1.	Location and Funding	Southampton General Hospital, England. Medical Research Council; University of Southampton; British Heart Foundation; Foods Standards Agency.
2.	Objectives of Study	To examine how variations in milk feeding and the weaning diet relate to body composition at age 4.
3.	Study Design	Prospective Cohort
4.	Number of and Description of Subjects	536 Children, aged 4. 277 boys and 251 girls.
5.	Variables Measured	**Maternal characteristics**, including educational attainment, BMI and smoking in late pregnancy- through pre-pregnant interview; **Age of introduction of solids**- through food frequency questionnaire at 6 and 12mths via an interview; **Duration of breastfeeding**- as above; **Body Composition:** Dual x ray absorptiometry (DEXA) scan- Hologic 4500 Discover W Instrument; Height – portable, Leicester height measure; Weight in underwear- calibrated digital SECA scales
6.	Age at measurement	6mths; 12mths; DEXA age 4.
7.	Definition of Obesity	International Obesity Task Force BMI>25kg/m^2 overweight, BMI >30kg/m^2 obese.
8.	Duration of Study	4years
9.	Statistics Analysed	Continuous variables were compared between 2 groups using *t* tests, and associations between the two categorical variables were assessed using x^2 tests. Pearson's correlation coefficients used to assess association between two continuous variables and multivariate analysis was performed using linear regression.

	Skewed variables were given interquartile ranges (IQR). Univariate association between infant feeding variables and measure of body fat at age 4 were consider after taking account of confounding factors, scores divided into quartiles.
10. Results	Median duration of breastfeeding was 15wks. Median age of introduction of solids were17.5wks (guidance mths/24wks). Birth weights of boys was higher than those of girls (p=0.003). 84% of children had normal BMI at age 4; 13% overweight and 3% obese. Breastfeeding duration was shorter among the overweight and obese children (median 8.7wks). Weak inverse relationship between fat mass at age 4 and introduction of solids (p=0.034), association no longer seen after adjustment for confounding factors. BMI, fat mass index, lean mass, and lean mass index were not related to age at introduction of solids. BMI, fat mass index, fat mass index were not associated with infant feeding score. However, a positive association lean mass and lean mass index was seen (not changed following adjustment for confounding factors (lean mass - p=0.001/ adjusted 0.003 and lean mass index- 0.011/ 0.004).
11. Conclusions	Adherence to current recommendations to breastfeed and to provide a weaning diet based on fruit, vegetables and home prepared foods is associated with a higher lean mass and lower fat mass at age 4.
12. Full Reference	Robinson, S.M., Marriott, L.D., Crozier, S.R., Harvey, N.C., Gale, C.R., Inskip, H.M., Baird, J., Law, C.M., Godfrey, K.M., Cooper, C., & Southampton Women's Survey Study Group. 2009. Variations in infant feeding practice are associated with body composition in childhood: a prospective cohort study. *The Journal of Clinical Endocrinology and Metabolism*. 94 (8), 2799-2805.

Appendix B: Study Summary Sheets continued

Author (s): Butte (2008)
Title: Impact of Infant Feeding Practices on Childhood Obesity

1.	Location and Funding	USDA/ARS Children's Nutrition Research Centre, Department of Paediatrics, Baylor College of Medicine, Houston, Texas 77030
2.	Objectives of Study	Identify genetic and environmental factors affecting obesity and its co morbidities.
3.	Study Design	Longitudinal Study- Prospective
4.	Number of and Description of Subjects	1030 Hispanic Children form 319 families (between Nov 2000– Aug 2004). Overweight Children, aged between 4- 19years.
5.	Variables Measured	Exclusive breastfeeding Partial breast feeding Breastfeeding duration Age of introduction of solid food Total energy intake Dietary Fat (% of energy) Diet carbohydrate (% of energy) Dietary protein (% of energy) Dinner test meal (kJ) Eating in absence of hunger (kJ)- food diary
6.	Age at measurement	Between 4-19 years.
7.	Type of assessment tool used to identify overweight/ obesity	Centers for Disease Control as percentile for BMI>95 2x 24hr diet recalls- parental/ individual
8.	Duration of Study	4 years
9.	Statistics Analysed	Odds Ratio for potential risk factors Binary logistic regression
10.	Results	Solid foods were introduced at mean of 5.1+/- 0.1 month for all cases. The age of introduction of solids was not related to the risk of obesity.

	Total energy intake (p=0.003) was positively associate with risk of childhood obesity as was ad libitum energy intake at dinner and amount of energy consumed in the absence of hunger. Carbohydrate intake (p-0.03) was inversely related to the risk of obesity
11. Conclusions	As well as breastfeeding and infant feeding other genetic and environmental risk factors exist such as parental obesity, smoking, birth weight, and rapid infancy weight gain far supersede infant feeding practices.
12. Full Reference	Butte, N.F. (2008) Impact of infant feeding practices on childhood obesity. *The Journal of Nutrition*, 139/2,412S-6S). Retrieved from http://jn.nutrition.org

Appendix B: Study Summary Sheets continued

Author (s): Griffiths et al. (2009)

Title: Effects of infant feeding practice on weight gain from birth to 3 years

1. Location and Funding	MRC Centre of Epidemiology for Child Health, UCL Institute of Child Health, London, Department of Epidemiology and Population Health, London, London School of Hygiene and Tropical Medicine, London. ESRC and consortium of government funders.
2. Objectives of Study	To examine the effect of breastfeeding initiation, breastfeeding duration and age at introduction of solids on weight gain from birth to 3yrs.
3. Study Design	Prospective Cohort
4. Number of and Description of Subjects	10,533 3 year olds. UK (England, Wales, Scotland and Northern Ireland. Excluded: ethnic minority children, multiple conceptions, dual families, not born full term, implausible weight at birth.
5. Variables Measured	**Birth weight** (kg)- converted into z scores based in 1990 growth references. **Family factors (including education/ BMI etc), infant feeding and child's birth weight**- via survey interview at 9mths. **Weight (kg) and height (m)-** trained interviewers, no shoes, or outdoor clothing. Tanita HD-305 scales (Tanita UK) and Leicester Health Measure Stadiometers (SECA ltd Birmingham).
6. Age at measurement	9mths survey interview. 3years- weight, height and survey interview.
7. Definition of Obesity	1990 growth reference charts.
8. Duration of Study	Sept 2000 to January 2002 (initial phase) Sept 2003- April 2005 (second phase)
9. Statistics Analysed	STATA/SE 9.2. Results were calculated using sample and non response weight and survey commands, allowing for cluster sampling deign effect of MCS and attribution between contacts. Association between condition weight gain and each infant feeding practice were tested by linear regression (adjusted for confounding factors).

	All associations were adjusted for height a scores.
10. Results	39% of participants introduced solids before 6 mths. Conditional weight gain was also significantly associated with breast feeding duration p=0.003 (remained after adjustment for age of introduction of solids and height score- p=0.03) Conditional weight gain was also associated with age at introduction of solids p=<0.001 (with and without adjustment for confounding factors p=0.005), however this was not seen after adjustment for height z score p=0.8. Children breastfed for at least 4mths gained on average 11.86kg whereas those breastfed for less than 4mths gained on average 12.08kg (0.22kg (CI 0.11-0.33)). Children who were never breastfed or who breast milk is rapidly replaced by formula or solids, may have higher total energy and protein intake which stimulates greater fat deposition via greater insulin resistance. Children introduced to solids early were heavier but not fatter at age 3.
11. Conclusions	Infants of mother who adopted infant feeding practices not in accordance with the DH 1994 guidelines (weaned at 4mth) gained weight more rapidly.
12. Full Reference	Griffiths, L.J., Smeeth, L., Sherburne Hawkins, S., Cole, T.J., Dezateux, C. 2009. Effects of infant feeding practice on weight gain from birth to 3 years. *Archives of Diseases of Childhood, 94*, 577-582.

Appendix B: Study Summary Sheets continued

Author (s): Reilly et al. (2005)

Title: Early life risk factors for obesity in childhood: cohort study

1. Location and Funding	United Kingdom Scottish Executive Health Department; Medical Research Council; UK Government Departments; Wellcome Trust; US National Institute of Health; Medical Research Companies; Commercial Companies, Iranian Ministry of Health and Medical Education.
2. Objectives of Study	To identify the risk factors in early life (up to 3year) for obesity in children in the UK.
3. Study Design	Prospective Cohort
4. Number of and Description of Subjects	8234- 3934 males, 3824 females from UK.
5. Variables Measured	**Potential confounders**- via self reported at 32 weeks gestation; **Birth weight**- measured in delivery room ; **Infant feeding**- child questionnaire 6mths post partum; **Age at introduction of solids**- child questionnaire 6mths post partum; **Dietary patterns**- Food frequency questionnaire at 38mths;

	Weight- 8mths and 18mths (standard deviation score); **Rapid catch up growth 0-2yrs**- weight gain of >0.67 standard deviation scores in first 2yrs; **Adiposity rebound**- change in BMI up to 60mths; **Weight gain in first 12 mths**- calculated from variable weight at 12mths minus birth weight.
6. Age at measurement	As identified above.
7. Definition of Obesity	1990 growth reference charts.
8. Duration of Study	7years
9. Statistics Analysed	Multivariable analysis for the prevalence of obesity in 3 stages using multivariable binary logistic regression models. To reduce the risk of producing misleading estimates for the variables, putative risk factors were analysed for childhood obesity simultaneously within each of the four risk groups (intrauterine and perinatal factors, weaning, family characteristic and demography, lifestyle in early childhood). For those risk factors which were independently significant within the groups a final simultaneous analysis was completed including adjustment for confounding factors- gender, maternal education, food groups. Growth related factors were assessed using binary logistic regression model controlling for other statistically significant risk factors.

10. Results	Following adjustment, the timing of the introduction of complementary food was not independently associated with the risk of obesity at age 7 (p=0.296). Dietary patterns- no conclusive evidence of an association with datary patterns at age 3 and risk of obesity at age 7. A junk food type diet was associated with risk of obesity at age 7 (although on to significance level of 10% p=0.83).
11. Conclusions	There is a role of early life environment in later obesity. Prevention strategies for childhood obesity to date have usually been unsuccessful and typically focus on change in lifestyle during childhood or adolescence. Future intervention might focus on environmental changes targeted at relatively short periods in early life, attempting to modify factors in utero in infancy, or early childhood which are independently related to later risk of obesity.
12. Full Reference	Reilly, J.J., Armstrong, J., Dorosty, A.R., Emmett, P.M., Ness, A., Rogers, I., Steer, C. & Sherriff, A. (2005). Early life risk factors for obesity in childhood: cohort study. *BMJ,* doi:10.1136/bmj.38470.670903.EO (published 20 May 2005).

Appendix B: Study Summary Sheets continued

Author (s): Baker et al. (2004)

Title: Maternal prepregnant body mass index, duration of breastfeeding, and timing of complementary food introduction are associated with weight gain.

1.	Location and Funding	Cornell University; Centre for Food Research, The Royal Veterinary and Agricultural University, Denmark; Danish Epidemiology Science Centre; Institute of Preventative Medicine, Copenhagen University Hospital. Einaudi Centre at Cornell University.
2.	Objectives of Study	To examine the associations between prepregnant body mass index and infant feeding patterns on infant weight gain.
3.	Study Design	Prospective observational study
4.	Number of and Description of Subjects	5845 sample (prior to exclusions- excluded for: low birth weight, early gestation, illnesses that affect growth, under 18yrs, never breastfed, alternative form of breastfeeding, diabetes). Therefore final sample of 3768 pairs used. Danish National Birth Cohort (DNBC), national cohort of mother and infant dyads established in 1996. Women were identified to participate by their GP at wk 12 of pregnancy, were from Denmark and spoke Danish. Women were interviewed by telephone 4 times: 12 weeks gestation; 26weeks gestation: 6mth postpartum; 18mth postpartum.
5.	Variables Measured	Maternal variables (e.g. SES, Education, age, occupation, parity, self reported height and weight etc)- at 12wk interview. Maternal health conditions, alcohol use, smoking habits during pregnancy- at 12 and 26wk gestation and 6mth postpartum interviews. Gestational weight gain- self reported at 6mths postpartum. Family income (expressed as a continuous variable)- via 18mth postpartum interview. Infant Feeding Variable: Current feeding practices and duration of breastfeeding, use of formula (ever fed) and introduction of complementary food – 6mth postpartum interview.

	Duration of breastfeeding and use of formula feeding- 18mths postpartum. All analyses on breastfeeding are based on the total duration of feeding in wks. Age at introduction of complementary foods (age complementary foods were first fed). Infant Variables: Duration of Gestation- LMP at 12wk interview of by date scan- followed by gestation estimates due to the two techniques used. Infant birth weight- obtained from Danish birth registry. Weight and length at 1yr- obtained from maternal report from green book at 18mth postpartum interview. Weight gain calculated from infant weight at doctors 1yr visit minus birth weight.
6. Age at measurement	Birth and 1year.
7. Definition of Obesity/ • Weaning guidance followed	N/a and looking at weight gain/ weight changes. Danish Governments recommendation 4-6mths.
8. Duration of Study	
9. Statistics Analysed	Timing of complementary foods (continuous variable) differed by quartiles of any breastfeeding duration- ANOVA. To compare the timing of complementary food introduction among categories of breastfeeding duration with those who breastfed for the longest duration (>40wks) Dunnett's t test was used. Students t test was used to test whether the timing of complementary food introduction was similar between women who never fed formula to their infants by 6mths and those that did. Linear regression was used to test whether any interaction between the categories of any breastfeeding duration and the category of infant formula use by 6mth of age on the timing of complementary food introduction.
10. Results	55% had been given complementary food by 16wks and by 24 wks 99% had been given complementary foods. Women who breastfed the longest (>40wks) introduced complementary foods the latest. Those who breast fed for <20wks introduced complementary foods 2.4wks earlier and

	those who breastfed for 20-31.9wks introduced them 1.7wks earlier and those 32-40wks introduced them 0.8wks sooner (p=0.001). Formula fed infants were introduced solids 1.4wks earlier than those who were never fed formula (p=0.0001). Infants who were fed complementary foods at >16wks compared with those who were fed before 16wks gained 224.2g more from birth to 1 yr. Following investigation to see if there was an association between birth weight and age at introduction of solids no association was seen (p=0.5).
11. Conclusions	Infant weight gain is associated with maternal prepregnant BMI and with an interaction between the duration of breastfeeding and the timing of complementary food introduction.
12. Full Reference	Baker, J.L., Michaelsen, K.F., Rasmussen, K.M. & Sorensen, T.I.A. (2004). Maternal prepregnant body mass, duration of breastfeeding, and timing of complementary food introduction are associated with infant weight gain. *The American Journal of Clinical Nutrition,* 80, 1579-1588.

Appendix B: Study Summary Sheets continued

Author (s): Huh, et al. (2011)
Title: Timing of solid food introduction and risk of obesity in preschool aged children.

1. Location and Funding	USA Funded by National Institutes of Health (NIH)
2. Objectives of Study	Examine the association between timing of introduction of solid foods during infancy and obesity at 3yrs of age.
3. Study Design	Prospective birth cohort
4. Number of and Description of Subjects	847 children Massachusetts Excluded: did not speak fluent English; gestational age of less than 22wks; singleton pregnancy.
5. Variables Measured	**Birth weight and 4mth weight**- obtained from clinical records. **Height**- 3yrs using stadiometer (Shorr Productions, Olney). **Weight**- 3yrs using SECA 881 digital scales (SECA, Hanover). **BMI**- calculated. **BMI z scores** calculated using US National Reference Data. **Subscapular and triceps skinfold thickness**- using Holitan callipers (Holitan Ltd, UK). **Change in weight for 0-4mth**- calculation of the weight for age z scores at birth and 4mths. **Feeding Practices** including introduction of complementary foods via questionnaires. **Confounding factors**: maternal race and ethnicity; age; education and household income; mothers reported pre pregnancy weight and height and the paternal weight and height.
6. Age at measurement	**Infant Feeding practices**- birth, 6mths, 2 yrs and 3yrs. **Length/ height/ weight**- birth, 6mths and 3 yrs. **Skinfold thickness**- 3yrs.
7. Definition of Obesity	Obesity: 95th percentile or higher for age/ gender. <85th percentile for normal weight for age and gender.
8. Duration of Study	Recruitment between 1999-2002 (follow up until children were

	3yrs)
9. Statistics Analysed	Unadjusted and multivariable logistic and linear regression models were used to assess the association of the timing of the introduction of solids with obesity, BMI z scores and skinfold thickness. Breast and formula feeding models were adjusted for confounding factors. As were weight for age z scores for 0-4mths. Confounders that did not change estimates were excluded (birth weight, birth weight for gestational age z scores, gestational age at delivery, gestational weight gain).
10. Results	At 4mths 67% of children were breastfed (33% formula fed). 36% of formula fed infants were never breastfed and the remainder were breastfed for less than 4mths. 8% of breastfed infants commenced complementary foods before 4mths and 33 % of formula fed infants. Breast and formula infants had similar mean birth weights. Weight for length z scores from 0-4mths was substantially larger for formula fed than breastfed infants (0.54 vs 0.35 U; p=0.01). Breastfed infants the timing of solids was not associated with the odds of obesity. Breastfed infants who received solid foods between the age of 4 and 5 mths compared to those fed before 4mths did not have an increase risk of obesity at age 3yrs (OR:1.0 (95% CI: 0.3-3.3- unadjusted), following adjustment for weight for age z scores from 0-4mths this did not change. Formula fed infants who received solids before 4mths compared to those fed 4-5mths had a six fold increase in the odds of obesity at 3yrs (OR:6.3, 95% CI 2.3-16.9- adjusted). Formula fed after 6mths had a 3.6fold increase in the odds of obesity after adjustment for covariates but wide C (95%, 0.8-16.3). Formula fed infants weaned before 4mth had higher age 3 BMI z scores of 0.36 unit increment (95% CI:0.10-0.61). No association with sum of skinfolds at age of 3yrs for either formula or breastfed infants.
11. Conclusions	Among formula fed infants or infants weaned before the age of 4mths, introduction of solid foods before the age of 4mths was associated with increased odds of obesity at 3yrs of age.
12. Full Reference	Huh, S.Y., Rifas-Shipman, S.L., Taveras, E.M., Oken, E. & Gillman, M.W. 2011. Timing of solid food introduction and risk of obesity in preschool aged children. *Pediatrics,* 127, 544-551.

Appendix B: Study Summary Sheets continued

Author (s): Balaban et al. (2010)

Title: Early weaning and other potential risk factors for overweight among preschool children

1. Location and Funding	Brazil, South America No detail of funding
2. Objectives of Study	Investigate whether early weaning constitutes risk factors for overweight among preschool children.
3. Study Design	Case control
4. Number of and Description of Subjects	366 children (176 boys, 190 girls) Aged 2-6yrs from attending private schools in Brazil.
5. Variables Measured	Weight: no info Height: no info BMI calculated. birth weight- via questionnaire maternal BMI- via questionnaire factors relating to child's current diet - via questionnaire factors relating to children's current physical activity levels via questionnaire SES- via questionnaire Breastfeeding duration - via questionnaire
6. Age at measurement	Not stated
7. Definition of Obesity	85th percentiles for overweight (CDC, US growth reference charts,2000)
8. Duration of Study	Not stated
9. Statistics Analysed	Epi-Info version 6 and SPSS version 8.0 software used. Univariate analysis completed initially to determine individual variables are a risk factor for overweight. Multivariate regression used to compare all variables. 95% confidence levels used. Power 80%.
10. Results	Early weaning (<16wks) compared to >16wks) and risk of overweight: 1.42 OR (0.86-2.34) p=0.02 (unadjusted) (p=0.17

	adjusted).
11. Conclusions	The association between early weaning (receiving exclusive or predominant breastfeeding for less than 16wks) and overweight did not reach statistical significance following multivariate analysis.
12. Full Reference	Balaban, G., Motta, M, E, F, A., Silva, A. A. P. 2009. Early weaning and other potential risk factors for overweight among preschool children. *Clinics*, 65 (2), 181-187.

Appendix B: Study Summary Sheets continued

Author (s): Hoppe et al. (2004)

Title: Protein intake at 9mths of age is associated with body size but not with body fat in 10yr old Danish children

1. Location and Funding	Denmark Funded: Danish Medical Research Council, Danish Medical Association Research Fund, The Society for the Prevention of Cardiovascular Diseases.
2. Objectives of Study	To examine the association between protein intake in infancy and body size and composition in late childhood.
3. Study Design	Observational Cohort
4. Number of and Description of Subjects	105 children examined at 9mth and 10yrs
5. Variables Measured	Weight- electronic scales (no detail given) Length- 9th using wooden measuring board, 10yr using wall mounted stadiometer. Tricep and subscapular thickness- using Harpenden Skinfold calliper (Chasmors Ltd, London); Duel x ray absorptiometry scanning (DEXA) at 10yrs- using Hologic 1000/w (Hologic Inc, Waltham, MA). Puberty assessment- using Tanner methods. Food intake- at 9mth and 10yrs using 5 and 7day food record chart. Blood analyses – 9mth and 10yrs using fasting sample.
6. Age at measurement	Weight at 9mth and 10yrs Length at 9mths and 10yrs Tricep and subscapular thickness at 9mths and 10yr Duel x ray absorptiometry scanning (DEXA) at 10yrs
7. Definition of Obesity	IOTF definitions based on BMI at 18yr
8. Duration of Study	10yrs (follow up took place in 1997/98)
9. Statistics Analysed	SPSS (version 11, SPSS Inc, Chicago) Differences in descriptive variables between boys and girls – Mann Whitney test.

	Pairwise partial correlations with adjustment for sex between diet, anthropometric and bloods variable in infancy and childhood. Multiple linear regression used for anthropometric measurements at 10yrs (%BF. BMI, weight, height) on each protein variable at 9mth (controlled for sex).
10. Results	1% increase in protein intake at 9mths is associated with an increased weight at age 10yrs of approximately 0.44kg. 1% increase in protein intake at 9mths is associated with increased length at age 10yrs of approximately 0.51cm (p=0.009). Protein intake at 9mth was not significantly associated with %BF at 10yrs (p value not given)
11. Conclusions	High protein intake stimulates early growth. Possible explaining the association between early PI and body size at 10yrs, however, the continuous effect of protein on growth during childhood cannot be excluded. PI was not associated with any measure of body fat at age 10yrs.
12. Full Reference	Hoppe, C., Molgaard, C., Thomsen, B.L., Juul, A. & Michaelsen, K.F. 2004. Protein intake at 9mo of age is associated with body size but not with body fat in 10y-old Danish children. *American Journal of Clinical Nutrition,* 79, 494-501.

Appendix B: Study Summary Sheets continued

Author (s): Scaglioni et al. (2000)

Title: Early macronutrient intake and overweight at five years of age.

1. Location and Funding	Italy Funding- no information detailed.
2. Objectives of Study	To examine the influence of the macronutrient intake in early life on the development of overweight in children.
3. Study Design	Longitudinal cohort
4. Number of and Description of Subjects	147 children (80 females/ 84 males) from birth to 5years
5. Variables Measured	Weight (kg)- Sartorius electric scales; Length (cm)- instrument used at birth not recorded, Harpen stadomiter (age 5yrs); Infant feeding practices- via interviews using food frequency questionnaires; Infant BMI- Overweight: 90th centile (age and sex adjusted Rolland-Cachera curves) Parental height and weight; Parental BMI- calculated using weight (kg)/height (m^2).
6. Age at measurement	Birth- weight, length; 1year- weight, length and feeding practices; 5yrs- weight, length and feeding practices.
7. Definition of Obesity	Overweight: 90th centile (age and sex adjusted Rolland-Cachera curves)
8. Duration of Study	5years
9. Statistics Analysed	Descriptive statistics results used means and SD, Odds ration and 95% confidence intervals calculated. Students t test and Wilcoxon and Mann Whitney tests used to compare differences between groups of continuous variables. Fisher's exact and chi square used to compare discrete variables. Multiple logistic analysis carried out to estimate the independent contribution of macronutrient intake at age 1 on overweight at age 5yrs.

	All factors with p=<0.05 at univariate analysis were analysed by multivariate regression and adjusted for confounders. Significance = p=0.05. SPSS 7.5 for windows used (SPSS Inc, Chicago, IL, USA).
10. Results	Nutrient (energy %) Proteins- p=0.024 CHO- p= 0.031 Fat- p=0.728
11. Conclusions	Parental overweight is a major risk factor for childhood overweight in the first years of life, but an early high protein intake may also influence the development of adiposity.
12. Full Reference	Scaglioni, S., Agostoni, C., De Notaris, R., Radelli, G., Radice, N., Valenti, M., Giovannini, M. & Riva, E. 2000. Early macronutrient intake and overweight at five years of age. *International Journal of Obesity,* 24, 777-781.

Appendix B: Study Summary Sheets continued

Author (s): Gunnarsdottir & Thorsdotti. (2003)

Title: Relationship between growth and feeding in infancy and body mass index at the age of 6 years

1. Location and Funding	Iceland Funding: not detailed.
2. Objectives of Study	To assess the relationship between size and growth measurements in infancy to body mass index at 6years.
3. Study Design	Longitudinal Cohort study
4. Number of and Description of Subjects	90 children, 41 males, 49 females. Healthy, full term.
5. Variables Measured	Weight (kg)- scales used not detailed. Height (cm)- measure used not detailed. Food intake- via monthly food diaries during infancy and then at 2,4, 6, 9, 12 mths weighed food diaries. Phillips HR 2385 (Austria) scales used to weigh foods.
6. Age at measurement	Weight- birth (retrospective gathering of data from infant birth records- data dredging), 12mth and 6yrs. Height- birth (retrospective gathering of data from infant birth records- data dredging), 12mth and 6yrs. Food intake- as above.
7. Definition of Obesity	IOTF definitions based on BMI at 18yr
8. Duration of Study	6years
9. Statistics Analysed	Variables used in analysis were tested for normality using Kolmogorov- Smirnov test (less than 100 subjects). Univariate linear regression was used to assess relationship between size and growth variables and BMI at age 6yrs. Multi linear regression used to assess the relationship between energy giving nutrient intake in infancy and total energy intake at varying ages. Multiple linear regression used to compare independent variables which correlated strongest with BMI at age 6yrs. One way ANOVA and Bonferroni post hoc test used to asses' difference in BMI between and quartiles of protein intake in infancy. T test used to assess difference between two independent

	groups. SPSS version 11 for windows (SPSS Inc, Chicago, IL, USA). Comp-Eat Nutritional System (Carlston Bengtson Consultants Ltd, London).
10. Results	Weight gained during the first 12mths as a ratio of birth weight was positively related to BMI at age 6yrs for both boys and girls (b= 2.9+/- 1.0, p=0.008, girls= 2.0+/-0.9, p=0.032). Boys in the highest quartile of protein intake (% of energy) at age of 9-12mths had significantly higher BMI (17.8+/-2.4kg/m^2) at age 6yrs that the lowest quartile (15.5+/-1.0kg/m^2) and the second lowest (15.3+/-0.8kg/m^2). No variation between energy consumption within the group. Weight gain at 1-12mths and protein intake at 9-12mths explained 50% of the variance in BMI among 6yr old boys.
11. Conclusions	Rapid growth during the first year of life is associated with increased BMI at the age of 6yrs in both genders. In boys, high intake of protein in infancy could also contribute to childhood obesity.
12. Full Reference	Gunnarsdottir, I. & Thorsdotti, I. (2003). Relationship between growth and feeding in infancy and body mass index at the age of 6years. *International Journal of Obesity,* 27, 1523-1527.

Appendix B: Study Summary Sheets continued

Author (s): Günther et al. (2007)

Title: Protein intake during the period of complementary feeding and early childhood and the association with Body Mass Index and percentage body fat at 7yrs of age.

1. Location and Funding	Germany Funding: Ministry of Science and Research of North Rhine Westphalia, Germany and International Foundation for the Promotion of Nutrition Research and Nutrition Education.
2. Objectives of Study	To see if there is an association between different protein intakes during 6-24mths with BMI and percentage body fat at 7years of age.
3. Study Design	Longitudinal cohort
4. Number of and Description of Subjects	203 children (104 boys/ 99 girls) Aged: birth to age 7yrs
5. Variables Measured	Birth Weight (kg)- via supine infant weighing scales (PS15, Mettler, Columbus, OH) Weight (kg)- via electronic scales (SECA 753, Hamburg, Germany) Height (cm)- via Harpenden stadiometer (Holitan, Crymych, UK) Scapular and Triceps thickness- via Holtain calliper. BMI calculated and sex dependant scores given (SDS) Food Intake- via 3day weighed food records measured to nearest g (Soehnle Digital 8000 scales). Confounders (e.g. maternal educational attainments, weight etc)- via questionnaire/ interview
6. Age of measurement	Birth Weight (kg)- at each visit age not specified Weight (kg) - at each visit age not specified Height (cm) - at each visit age not specified Scapular and Triceps thickness- 6mths, 12mths, 18mths, 24mths. Food Intake- 6, 12, 18 & 24mths.
7. Definition of Obesity	IOTF definitions based on BMI at 18yr
8. Duration of Study	Not specified

9.	Statistics Analysed	Descriptive statistics analysed across the 4 dietary protein groups (LL, LH, HL, HH). Differences between groups were analysed using analysis of variance or Kruskal-Wallis tests for continuous data and chi square for categorical data. Analysis of covariance and calculated adjusted odd ratio to compare adjusted BMI SDS and %BF at 7yrs according to protein intakes using logistic regression model. Univariate analysis was completed for confounders and in full models. SAS version 8.2 used (SAS Institute Inc, Cary, NC). Significance set at p=<0.05. Power of 80% (2 tailed)
10.	Results	Protein intakes differed from between the low and high intake groups at 6mths (7-8% of energy compared to 12%) and 12mths (11-12% of energy compared to 14-15%). No variation at later ages. High protein intake at 12mth was associated with a higher BMI SDS at age 7yrs (p=0.02), similar results seen for %BF (p=<0.0001).
11.	Conclusions	High protein intake during the period of complementary feeding and the transition to the family diet are associated with an unfavourable body composition at age 7yrs.
12.	Full Reference	Günther, A.L.B., Buyken, A.E. & Kroke, A. 2007. Protein intake during the period of complementary feeding and early childhood and the association with body mass index and percentage body fat at 7yr of age. *The American Journal of Clinical Nutrition,* 85, 1626-1633.

Appendix C1: Master Table of Results- Age of weaning on weight gain and/ or overweight/ obesity in children

Author and Title	Date	Location	Study Design	Subjects (n)[a]	Overweight/ Obesity Classification [b]	Measurements [c]	Number of children weaned early and Age of Weaning (wks/mths)	Infant Feeding Guidelines Followed [d]	Adjustments [e]	P value (or alternative)	Downs and Black Score	Findings [f]
Robinson et al Variations in infant feeding proactive are associated with body composition in childhood	2009	UK	Prospective birth cohort	536 children- 283 males, 253 females; 4yrs of age.	Overweight: BMI >25kg/m^2; Obese: BMI >30kg/m^2 (International Obesity Task Force)	Dual X ray absorptiometry; Weight (kg); Height (m); BMI (kg/m^2)	536 <6mths Mean age of introduction 17.5 wks	2006 DH Birth to Five- 6mths	Sex; Maternal age; BMI; Height; Education; Social Class; Smoking in late pregnancy; Infant birth weight; age of introduction of solids.	Fat mass at age 4 and age of introduction of solids: p=0.034 (adjustment- not significant). Infant feeding guideline score and lean mass (kg): P=0.001 (adjustment p=0.003); Infant feeding guideline score and lean mass index(kg/m2.5): P=0.011 (adjustment p=0.004).	20	No association between infant feeding guideline scores and BMI, fat mass, or fat mass index at age 4yrs. Lean mass and lean mass index positively associated with high infant feeding scores (diet based on fruit and vegetables, cooked meat and fish and other home prepared foods). Increased duration of breastfeeding (later weaning) associated with lower fat mass. No association between infant diet and mean BMI at age 4yrs.
Sloan et al Early weaning is related to weight and rate of weight gain in infancy	2007	Northern Ireland (UK)	Cohort	234- 119 males, 115 females; 0-18mths of age.	N/A	Weight Weight Gain	92 children <16wks	1994 DH Infant Feeding Recommendations- 4mths (16wks)	Breastfeeding	Birth z score: 0.150; 8 week: 0.555; 7mths: 0.005 *(adjustment- 0.046)*; 14mth: 0.004 *(adjustment= 0.035)*; 8wk-14mth wt gain: 0.003 *(adjustment- 0.029)*	18	Infants weaned early had higher weight z scores at age 7months and 14months. Early weaning related in greater weight gain between 8weeks and 14months.
Burdette et al Breastfeeding, introduction of complementary foods and adiposity at 5 years of age	2006	USA	Cohort	313 preschool children- 166 males of which 24 black), 147 (of which 40 black) females.	Overweight=>85th percentile; BMI measured kg/m^2.	Fat Mass- though Duel Energy X ray Absorptiometry; Height (m); Weight (kg); BMI- percentile and z score.	156 children < 16weeks	American Academy of Pediatrics (AAP) recommendation- 4mths (16wks)	Breastfeeding; **Childs:** Lean Body Mass; Sex; Race; Birth weight; **Maternal:** Obesity; Smoking; Age; Marital status; Education; Gestational diabetes	Breastfeeding, formula feeding and use of complementary foods in first 4mths (16wks): never breastfed: p= 0.51; Partially breastfed: p= 0.39; Exclusively breastfed: p= 0.45.	19	No significant relationship between adiposity (DXA) at age 5yrs and either breastfeeding or the timing of the introduction of complementary foods (following adjustment for cofounders).
Griffiths el al Effects of infant feeding practice on weight gain from birth to 3 years	2009	UK	Prospective birth cohort	10,553 children- 5295 males, 5239 females; 3yrs of age from UK.	1990 growth references	Weight (kg); Height (m)	4134 (39%)	1994 DH Infant Feeding Recommendations- 4mths (16wks)	Height; Maternal SES; Maternal body size; Birth weight; Age; Gender; Socioeconomic status; Education; Prepregnancy BMI; Parity; Smoking during pregnancy.	Solids before 4 mths: p= <0.001 (adjusted p=0.003).	21	Conditional weight gain was associated with age at the introduction of solids (following additional adjustment for height association no longer existed).

Appendix C1: Master Table of Results- Age of weaning on weight gain and/ or overweight/ obesity in children Continued

Author and Title	Date	Location	Study Design	Subjects (n)[a]	Overweight/ Obesity Classification [b]	Measurements [c]	Number of children weaned early and Age of Weaning (wks/mths)	Infant Feeding Guidelines Followed [d]	Adjustments [e]	P value (or alternative)	Downs and Black Score	Findings [f]
Reilly et al Early life risk factors for obesity in childhood: a cohort study	2005	UK	Prospective birth cohort	8234- 3934 males, 3824 females from UK.	1990 growth references- Obesity: >95th centile	Weight (kg); Height (m)	<1mth: 17; 1 or 2mth: 12; 2 or 3mth: 77; 3 or 4 mth: 320; 4-6mth: 134.	Not noted	Maternal SES; Gender; Energy intake of child.	Introduction of solids: p=0.003 (adjusted p=296).	19	Following adjustment, the timing of the introduction of complementary food was not independently associated with the risk of obesity at age 7. Dietary patterns- no conclusive evidence of an association with dietary patterns at age 3 and risk of obesity at age 7. A junk food type diet was associated with risk of obesity at age 7 (although on to significance level of 10% p=0.83).
Baker et al. Maternal prepregnant BMI, duration of breastfeeding, and timing of complementary food introduction are associated with infant weight gain	2004	Denmark	Prospective, observational cohort	3768	N/A	weight (g) length (cm)	2072 16wks	Danish Governments recommendation 16-24wks	Primiparity; gestational weight gain; duration of gestation; maternal cigarette smoking during pregnancy; infant sex; infant birth weight; infant length at age 1yr; infant age when the 1 yr measurements were taken; breastfeeding; complementary foods	early weaning (<16wks) compared to >16wks) and infant weight gain at 1yr p=0.0021	17	Women who breastfed the longest (>40wks) introduced complementary foods the latest. Those who breast fed for <20wks introduced complementary foods 2.4wks earlier and those who breastfed for 20-31.9wks introduced them 1.7wks earlier and those 32-40wks introduced them 0.8wks sooner (p=0.001). Formula fed infants were introduced solids 1.4wks earlier than those who were never fed formula (p=0.0001). Infants who were fed complementary foods at >16wks compared with those who were fed before 16wks gained 224.2g more from birth to 1 yr.
Huh et al. Huh et al. 2011 Timing of solid food introduction and risk of obesity in preschool aged children	2011	USA	Prospective birth cohort	847	Obesity: 95th percentile	Length; Height; Skinfold thickness	134 <16wks	Not noted	maternal education; household income; prepregnancy BMI; partnernal BMI; childs age; gender; race/ethnicity	Adjusted: Formula fed <16wks: OR: 6.3 (2.3-16.9) of obesity at 3yrs; BMI z score: 0.36 (0.10-0.61); Sum of triceps and subscapular skinfolds: 1.03 (-0.12-2.18). Breastfed <16wks: OR: 1.1 (0.3-4.4) of obesity at 3yrs; BMI z score: -0.19 (-0.49-0.11); Sum of triceps and subscapular skinfolds: -0.19 (-1.42-1.04).	19	For those infants never breastfed or stopped breastfeeding before 4mths of age introduction of solids was associated with a 6 fold increased odds of obesity at 3yrs of age. For those breastfed infants who were fed longer than 4mths timing of solids introduction was not associated with the odds of obesity.
Balaban et al. Early Weaning and other risk factors for overweight among preschool children	2010	South America	Case Control	366 children 176 male; 190 female;	85th percentiles for overweight (CDC, US growth reference charts,2000)	Height; Weight; BMI calculated	132 <16wks	Not noted	birth weight; maternal BMI; factors relating to childs current diet; factors relating to children's current physical activity levels; SES; Breastfeeding.	early weaning (<16wks) compared to >16wks) p=0.02 (unadjusted) (p=0.17 adjusted).	20	The association between early weaning (receiving exclusive or predominant breastfeeding for less than 16wks) and overweight did not reach statistical significance following multivariate analysis.

a : Subject (males/ females and author classification if appropriate).
b : Classification of overweight/ obesity used in relevant studies.
c : Refers to the key measurements taken as part of the study, for example, weight, weight gain, DEXA scan.
d : Refers to the infant feeding guidelines followed at the time of the study.
e : Notes any adjustment for confounding factors as part of the study.
f : States the key findings for the study which are significant (p= <0.05).

Appendix C2: Master Table of Results- Nutritional composition of the weaning diet on weight gain and/ or overweight/ obesity in children

Author and Title	Date	Location	Study Design	Subjects (n)[a]	Overweight/ Obesity Classification[b]	Measurements[c]	Age of introduction of Solids	Total Energy Intake (KJ/d)[d]	Dietary Fat (% of energy)[d]	Dietary Carbohydrate (% of energy)[d]	Dietary Protein (% of energy)[d]	Weight Gain (kg)[d]	Adjustments[e]	Downs and Black Score	Findings[f]
Butte, N.F. Impact of Infant Feeding Practices in Childhood Obesity	2009	USA	Cohort	1030 Hispanic Children Aged 4-19	Overweight- Centres for Disease Control BMI >95 percentile	Birth Weight (kg)	5.1 ± 0.2mth	p= 0.003	p=0.11	p=0.03	p=0.14	n/a	Birth weight; Gestational age; Gestational diabetes; Mother's age in pregnancy; Birth order; Parental educational attainment; Family income; Gender; Breastfeeding	14	Solid foods introduced at a mean age of 5.1 ± 0.2mth. Age of introduction of solids was not associated with the risk of obesity. Total energy intake, ad labium energy intake at dinner and amount of energy consumed in absence of hunger associated with increase risk of obesity. Inverse relationship between carbohydrate as a percentage of energy.
Hoppe et al. Protein intake at 9mths of age is associated with body size but not with body fat in 10yr old Danish children	2004	Denmark	Observational Cohort	143 children	IOTF definitions based on BMI at 18yr	Weight; Length; triceps and sub scapular thickness; Duel x ray absorptiometry scanning (DXA) at 10yrs	n/a	3088kJ/d = 349kJ/kg body wt	89g/d	286g/d	2.7g/d= 0.9-4.2g/kg body wt. P=0.007	n/a	Age; Gender	22	1% increase in protein intake at 9mths is associated with an increased weight at age 10yrs of approximately 0.44kg. 1% increase in protein intake at 9mths is associated with increased length at age 10yrs of approximately 0.51cm (p=0.009)
Scaglioni et al. Early macronutrient intake and overweight at five years of age	2000	Italy	Cohort (Longitudinal)	147 children (80 females/ 84 males)	Overweight: 90th centile (age and sex adjusted Rolland-Cachera curves)	Weight; Length.	4-6mth	p=0.663	p=0.728	p=0.031	p=0.024	n/a	Gender; Weight and length at birth and year 1; Parental age.	21	Parental overweight is a major risk factor for childhood overweight in the first years of life, but an early high protein intake may also influence the development of adiposity.
Gunnarsdottir et al. Relationship between growth and infant feeding and BMI at the age of 6years	2003	Iceland	Cohort (Longitudinal)	90 (41 boys /49 girls)	IOTF definitions based on BMI at 18yr	Birth Weight (kg);	not detailed	not significant (p value not given)	not significant (p value not given)	not significant (p value not given)	Boys 2mth- p= 0.003 4mth-p=0.027 6mth-not significant 9mth- p=<0.001 12mth- p=<0.001 Girls no significant difference at any age	Weight gain from birth to 12mths boys: p=0.008 girls: p=0.032	Gender; % Fat; % CHO; Total energy; Breastfeeding.	21	Rapid growth during the first year of life is associated with increased BMI at the age of 6yrs in both genders. In boys, high intake of protein in infancy could also contribute to childhood obesity.
Günther et al. Protein intake during the period of complementary feeding and early childhood and the association with body mass index and percentage body fat at 7years of age	2007	Germany	Longitudinal cohort	203 children (104 boys/ 99 girls) Aged: birth to age 7yrs	IOTF definitions based on BMI at 18yr	Birth Weight (kg) Weight (kg) Height (cm) Scapular and Triceps thickness	n/a	n/a	n/a	n/a	p=0.02	n/a	Gender; Maternal overweight; Maternal educational attainment; Gestational age; First born status; Smoking in the household; Breastfeeding at 6mths.	23	High protein intake at 12 mths of age is associated with a higher BMI SDS at 7yrs of age (p=0.02) and increased % body fat (adjusted for gender) (p=<0.0001). High protein intake during the period of complementary feeding and the transition to the family diet are associated with an unfavourable body composition at age 7yrs.

a : Subject (males/ females and author classification if appropriate).
b : Classification of overweight/ obesity used in relevant studies.
c : Refers to the key measurements taken as part of the study, for example, weight, weight gain, DEXA scan.
d : Refers to the significance of the association between the dietary factor and overweight/ obesity, for example dietary protein p=0.001.
e : Notes any adjustment for confounding factors as part of the study.
f : States the key findings for the study which are significant (p= <0.05).